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NEWS 8	NOV 20	CA/CAplus to MARPAT accession number crossover limit increased to 50,000
NEWS 9	DEC 01	CAS REGISTRY updated with new ambiguity codes
NEWS 10	DEC 11	CAS REGISTRY chemical nomenclature enhanced
NEWS 11	DEC 14	WPIDS/WPINDEX/WPIX manual codes updated
NEWS 12	DEC 14	GBFULL and FRFULL enhanced with IPC 8 features and functionality
NEWS 13	DEC 18	CA/CAplus pre-1967 chemical substance index entries enhanced with preparation role
NEWS 14	DEC 18	CA/CAplus patent kind codes updated
NEWS 15	DEC 18	MARPAT to CA/CAplus accession number crossover limit increased to 50,000
NEWS 16	DEC 18	MEDLINE updated in preparation for 2007 reload
NEWS 17	DEC 27	CA/CAplus enhanced with more pre-1907 records
NEWS 18	JAN 08	CHEMLIST enhanced with New Zealand Inventory of Chemicals
NEWS 19	JAN 16	CA/CAplus Company Name Thesaurus enhanced and reloaded
NEWS 20	JAN 16	IPC version 2007.01 thesaurus available on STN
NEWS 21	JAN 16	WPIDS/WPINDEX/WPIX enhanced with IPC 8 reclassification data
NEWS 22	JAN 22	CA/CAplus updated with revised CAS roles
NEWS 23	JAN 22	CA/CAplus enhanced with patent applications from India
NEWS 24	JAN 29	PHAR reloaded with new search and display fields
NEWS 25	JAN 29	CAS Registry Number crossover limit increased to 300,000 in multiple databases

NEWS EXPRESS NOVEMBER 10 CURRENT WINDOWS VERSION IS V8.01c, CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP), AND CURRENT DISCOVER FILE IS DATED 25 SEPTEMBER 2006.

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=> s (IGF(w)II or IGF(W)2 or insulin(w)growth(w)factor(w)II)
L1 20177 (IGF(W) II OR IGF(W) 2 OR INSULIN(W) GROWTH(W) FACTOR(W) II)

=> s l1 and placenta? and treatment
L2 136 L1 AND PLACENTA? AND TREATMENT

=> dup rem l2
PROCESSING COMPLETED FOR L2
L3 49 DUP REM L2 (87 DUPLICATES REMOVED)

=> dis ibib abs l3 1-49

L3 ANSWER 1 OF 49 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2007:16768 CAPLUS
DOCUMENT NUMBER: 146:119977
TITLE: Precursor platelet basic protein-derived CTAP3-related proteins as biomarkers for ovarian cancer discovered in ProteinChip array using SELDI
INVENTOR(S): Zhang, Zhen; Chan, Daniel W.; Fung, Eric Thomas; Wang, Zheng; Zhang, Fujun
PATENT ASSIGNEE(S): The Johns Hopkins University, USA; Ciphergen Biosystems, Inc.
SOURCE: PCT Int. Appl., 54pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2007002264	A2	20070104	WO 2006-US24269	20060621

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW

RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

PRIORITY APPLN. INFO.: US 2005-693324P P 20050622

AB The present invention provides a biomarker (a known protein CTAP3) that is useful in classifying a subject sample as ovarian cancer or non-ovarian cancer, and qualifying ovarian cancer status. The biomarker can be detected by SELDI mass spectrometry. It was found that CTAP3 (connective tissue activator peptide III), an 85 amino acid protein comprising amino acid residues 44-128 of PPBP (precursor platelet basic protein), is up-regulated in the serum of patients with ovarian cancer. The CTAP3 biomarker was discovered using SELDI technol. employing ProteinChip arrays from Ciphergen Biosystems. The CTAP3 biomarker differentially present in samples from early stage ovarian cancer vs. healthy controls; early stage ovarian cancer vs. post-operative cancer free (serial samples from patients before and after treatment), and early stage ovarian cancer vs. benign disease, either ovarian or non-ovarian disease. The invention also include biomarkers referred as "CTAP3-related proteins" that derived from PPBP including β-thromboglobulin and neutrophil-activating peptide-2 (CXCL7).

L3 ANSWER 2 OF 49 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2006:1311584 CAPLUS

DOCUMENT NUMBER: 146:55471

TITLE: Gene expression markers for the identification, assessment, and treatment, and responsiveness of cancer using proteasome inhibition or glucocorticoid therapy

INVENTOR(S): Bryant, Barbara M.; Damokosh, Andrew I.; Mulligan, George

PATENT ASSIGNEE(S): Millennium Pharmaceuticals, Inc., USA

SOURCE: PCT Int. Appl., 152pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006133420	A2	20061214	WO 2006-US22515	20060608
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
US 2006281122	A1	20061214	US 2006-449195	20060608

PRIORITY APPLN. INFO.: US 2005-688634P P 20050608

AB The present invention is directed to the identification of predictive markers that can be used to determine whether patients with cancer are clin. responsive or non-responsive to a therapeutic regimen prior to treatment. In particular, the present invention is directed to the use of certain individual and/or combinations of predictive markers, wherein the expression of the predictive markers correlates with responsiveness or non-responsiveness to a proteasome inhibition and/or a

glucocorticoid therapeutic regimen. A multicenter, open-label, randomized study was conducted comprising 627 enrolled patients with relapsed or refractory multiple myeloma treated with either bortezomib (Velcade®) or dexamethasone (Decodron®). Differentially expressed markers on Affymetrix U133 microarrays (A and B) were identified by using a combination of marker ranking algorithms, supervised learning, and feature selection algorithms. The expression levels of individual predictive markers, and/or predictive markers comprising a marker set, are correlated with a pos. or neg. response to therapy or a long time until disease progression.

L3 ANSWER 3 OF 49 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2006:795802 CAPLUS
DOCUMENT NUMBER: 145:246606
TITLE: Marker genes for the diagnosis of chronic fatigue syndrome by gene expression profiling
INVENTOR(S): Gow, John; Chaudhuri, Abhijit
PATENT ASSIGNEE(S): The University Court of the University of Glasgow, UK
SOURCE: PCT Int. Appl., 169pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006082390	A1	20060810	WO 2006-GB332	20060201

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

PRIORITY APPLN. INFO.: GB 2005-2042 A 20050201
AB Genes that show changes in levels of expression in chronic fatigue syndrome (myalgic encephalitis) are identified for use in the diagnosis of the disease and in its treatment. These genes include those encoding defensin α1, Hb γ, CXCR4, tubulin β1, serine/threonine kinase 17B, HLA-DRβ4, and prostaglandin D2 synthase. There is a relatively small set of genes, identified as a hub set, that show changes in expression that result in changes in levels of expression of a number of dependent or network genes. The genes identified provide objective disease markers that may be used in diagnostic tests to support the diagnosis of CFS/ME or for monitoring the effectiveness of therapy. They also provide a rational basis for classifying CFS/ME patients according to the biochem. lesion underlying their symptoms and enable provision of appropriate targeted therapies.
REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 4 OF 49 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2006:364726 CAPLUS
DOCUMENT NUMBER: 144:363110
TITLE: Methods of using adipose tissue-derived cells in the treatment of cardiovascular conditions
INVENTOR(S): Fraser, John K.; Hedrick, Marc H.; Zhu, Min; Strem, Brian M.; Daniels, Eric; Wulur, Isabella

PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 58 pp., Cont.-in-part of U.S. Ser. No. 877,822.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 15
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2006083720	A1	20060420	US 2005-138083	20050525
US 2003161816	A1	20030828	US 2002-316127	20021209
US 2005008626	A1	20050113	US 2004-783957	20040220
US 2005084961	A1	20050421	US 2004-877822	20040625
WO 2006022612	A2	20060302	WO 2004-US21483	20040701
WO 2006022612	A3	20060526		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

PRIORITY APPLN. INFO.:

US 2001-338856P	P	20011207
US 2002-316127	A2	20021209
US 2003-449279P	P	20030220
US 2003-462911P	P	20030415
US 2003-482820P	P	20030625
US 2003-496467P	P	20030820
US 2004-783957	A2	20040220
US 2004-877822	A2	20040625

AB Adipose derived regenerative cells are used to treat patients, including patients with cardiovascular conditions, diseases or disorders. Methods of treating patients include processing adipose tissue to deliver a concentrated amount of regenerative cells, e.g., stem and/or progenitor cells, obtained from the adipose tissue to a patient. The methods may be practiced in a closed system so that the stem cells are not exposed to an external environment prior to being administered to a patient. Accordingly, in a preferred method, adipose derived regenerative cells are placed directly into a recipient along with such additives necessary to promote, engender or support a therapeutic cardiovascular benefit.

L3 ANSWER 5 OF 49 MEDLINE on STN DUPLICATE 1
ACCESSION NUMBER: 2006363646 MEDLINE
DOCUMENT NUMBER: PubMed ID: 16556757
TITLE: Maternal insulin-like growth factors-I and -II act via different pathways to promote fetal growth.
AUTHOR: Sferruzzi-Perri Amanda N; Owens Julie A; Pringle Kirsty G; Robinson Jeffrey S; Roberts Claire T
CORPORATE SOURCE: Research Center for Reproductive Health, Discipline of Obstetrics and Gynecology, University of Adelaide, Adelaide, South Australia, Australia 5005.
SOURCE: Endocrinology, (2006 Jul) Vol. 147, No. 7, pp. 3344-55. Electronic Publication: 2006-03-23.
Journal code: 0375040. ISSN: 0013-7227.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English

FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 200607
ENTRY DATE: Entered STN: 17 Jun 2006
Last Updated on STN: 25 Jul 2006
Entered Medline: 24 Jul 2006

AB The placenta transports substrates and wastes between the maternal and fetal circulations. In mice, placental IGF -II is essential for normal placental development and function but, in other mammalian species, maternal circulating IGF -II is substantial and may contribute. Maternal circulating IGFs increase in early pregnancy, and early treatment of guinea pigs with either IGF-I or IGF-II increases placental and fetal weights by mid-gestation. We now show that these effects persist to enhance placental development and fetal growth and survival near term. Pregnant guinea pigs were infused with IGF-I, IGF-II (both 1 mg/kg.d), or vehicle sc from d 20-38 of pregnancy and killed on d 62 (term = 69 d). IGF-II, but not IGF-I, increased the mid-sagittal area and volume of placenta devoted to exchange by approximately 30%, the total volume of trophoblast and maternal blood spaces within the placental exchange region (+29% and +46%, respectively), and the total surface area of placenta for exchange by 39%. Both IGFs reduced resorptions, and IGF-II increased the number of viable fetuses by 26%. Both IGFs increased fetal weight by 11-17% and fetal circulating amino acid concentrations. IGF-I, but not IGF -II, reduced maternal adipose depot weights by approximately 30%. In conclusion, increased maternal IGF-II abundance in early pregnancy promotes fetal growth and viability near term by increasing placental structural and functional capacity, whereas IGF-I appears to divert nutrients from the mother to the conceptus. This suggests major and complementary roles in placental and fetal growth for increased circulating IGFs in early to mid-pregnancy.

L3 ANSWER 6 OF 49 MEDLINE on STN DUPLICATE 2
ACCESSION NUMBER: 2006435998 MEDLINE
DOCUMENT NUMBER: PubMed ID: 16862465
TITLE: Pregnancy-induced changes in insulin-like growth factor I (IGF-I), insulin-like growth factor binding protein 3 (IGFBP-3), and acid-labile subunit (ALS) in patients with growth hormone (GH) deficiency and excess.
AUTHOR: Wiesli Peter; Zwimpfer Cornelia; Zapf Jurgen; Schmid Christoph
CORPORATE SOURCE: Department of Internal Medicine, Division of Endocrinology and Diabetes, University Hospital of Zurich, Zurich, CH-8091, Switzerland.. peter.wiesli@stgag.ch
SOURCE: Acta obstetricia et gynecologica Scandinavica, (2006) Vol. 85, No. 8, pp. 900-5.
Journal code: 0370343. ISSN: 0001-6349.
PUB. COUNTRY: Denmark
DOCUMENT TYPE: (CASE REPORTS)
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200610
ENTRY DATE: Entered STN: 25 Jul 2006
Last Updated on STN: 18 Oct 2006
Entered Medline: 17 Oct 2006

AB BACKGROUND: Under most circumstances with altered growth hormone (GH) secretion, the changes of insulin-like growth factor I (IGF-I), insulin-like growth factor binding protein 3 (IGFBP-3), and acid-labile subunit (ALS) are in parallel. The aim of the present study was to compare the effects of pregnancy in a hypopituitary patient with those of pregnancy in an acromegalic patient on IGF-I, IGFBP-3, and ALS. METHODS

AND RESULTS: IGF-I and ALS were low before pregnancy in the hypopituitary patient under glucocorticoid and thyroxine treatment. Gonadotropin treatment allowed her to become pregnant; IGF-I and ALS levels rose in the second half of pregnancy and fell again after delivery. IGF-I concentrations were elevated in the patient with persistent acromegaly before and dropped into the normal range during the first half of pregnancy. In the second half of pregnancy and following delivery, IGF-I levels increased again. IGFBP-3 levels (as assessed by immunoblot analysis as well as by 125I-IGF II ligand blotting) decreased markedly during pregnancy in both patients, suggesting that the placenta rather than pituitary GH regulates IGFBP-3 proteolysis in human pregnancy. The increase of IGF-I (and ALS) during the second half of pregnancy in the individual with pituitary GH deficiency may be attributed to placental GH. The fall of IGF-I (and ALS) into the normal range in the acromegalic patient during the first trimester of pregnancy may be related to decreased production or decreased half-life of these proteins. CONCLUSION: Our data suggest that measures to continuously replace GH or to suppress GH secretion during pregnancy in patients with GH deficiency or excess, respectively, may not be warranted.

L3 ANSWER 7 OF 49 MEDLINE on STN DUPLICATE 3
ACCESSION NUMBER: 2006624458 IN-PROCESS
DOCUMENT NUMBER: PubMed ID: 16966353
TITLE: Altered placental and fetal expression of IGFs and IGF-binding proteins associated with intrauterine growth restriction in fetal sheep during early and mid-pregnancy.
AUTHOR: de Vrijer Barbra; Davidsen Meredith L; Wilkening Randall B; Anthony Russell V; Regnault Timothy R H
CORPORATE SOURCE: Department of Obstetrics and Gynecology, Division of Obstetrics and Prenatal Medicine, Erasmus University Medical Center, 3000 CB Rotterdam, The Netherlands.. bdevrije@uwo.ca
CONTRACT NUMBER: HD41505 (NICHD)
R01 HD20761 (NICHD)
SOURCE: Pediatric research, (2006 Nov) Vol. 60, No. 5, pp. 507-12. Electronic Publication: 2006-09-11. Journal code: 0100714. ISSN: 0031-3998.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE) (RESEARCH SUPPORT, N.I.H., EXTRAMURAL)
LANGUAGE: English
FILE SEGMENT: NONMEDLINE; IN-PROCESS; NONINDEXED; Priority Journals
ENTRY DATE: Entered STN: 24 Oct 2006
Last Updated on STN: 14 Dec 2006

AB The insulin-like growth factors (IGFs) are postulated to be altered in association with the development of intrauterine growth restriction (IUGR). The present studies examined placental and fetal hepatic mRNA concentration of components of the IGF system at two time points (55 and 90 d gestational age, dGA; Term 147 dGA) in a hyperthermia (HT)-induced sheep model of placental insufficiency-IUGR. Maternal plasma insulin and IGF-I were constant at 55 and 90 dGA and were unaffected by treatment. Umbilical vein insulin concentrations tended to be reduced at 90 dGA following HT exposure. Caruncle IGF-I mRNA was increased at 90 dGA in HT placentae ($p < 0.05$), while cotyledon concentrations were constant over gestation and unaltered by treatment. In control cotyledons, IGF-II mRNA concentration increased ($p < 0.01$) and IGFBP-3 decreased between 55 and 90 dGA ($p < 0.01$). Cotyledon IGF-II and caruncle IGFBP-4 mRNA were elevated at 55 dGA in HT placentae compared with control ($p < 0.01$ and $p < 0.05$ respectively). Fetal hepatic IGF-I, IGFBP-2, -3 and -4 concentrations rose over gestation ($p < 0.05$), but there were no treatment effects. These data suggest that

changes in placental IGF expression in early and mid gestation may predispose the pregnancy to placental insufficiency, resulting in inadequate substrate supply to the developing fetus later in gestation.

L3 ANSWER 8 OF 49 MEDLINE on STN DUPLICATE 4
ACCESSION NUMBER: 2006500362 MEDLINE
DOCUMENT NUMBER: PubMed ID: 16923367
TITLE: Effects of L-arginine on the expression of insulin-like growth factors and insulin-like growth factor binding protein 3 in rats with intrauterine growth retardation.
AUTHOR: Lu Yan; Liu Xiao-Mei; Li Shu-Qin
CORPORATE SOURCE: Central Laboratory, Second Affiliated Hospital of China Medical University, Shenyang 110004, China.
SOURCE: Zhongguo dang dai er ke za zhi = Chinese journal of contemporary pediatrics, (2006 Aug) Vol. 8, No. 4, pp. 319-22.
Journal code: 100909956. ISSN: 1008-8830.
PUB. COUNTRY: China
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: Chinese
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200610
ENTRY DATE: Entered STN: 23 Aug 2006
Last Updated on STN: 27 Oct 2006
Entered Medline: 26 Oct 2006

AB OBJECTIVE: Intrauterine growth retardation (IUGR) may contribute to the disorder of development of fetal brains. L-arginine has been known to be effective in blood vessel distension and improving the blood circulation of placentas. Recent studies have shown that L-arginine can ameliorate the placental hypoxia and improve the development of fetus. This study aimed to explore the effects of L-arginine on the expression of insulin-like growth factor (IGF)-I, IGF-II , IGF binding protein-3(IGFBP3)and IGF-I mRNA in brains of IUGR rats and the possible mechanisms of L-arginine. METHODS: Thirty-six pregnant rats were randomly assigned into four groups: Control, Model, Low dose L-arginine (100 mg/kg) and High-dose L-arginine (200 mg/kg L-arginine) groups (n=9 each). IUGR was induced by passive smoking in rats from the last three groups. L-arginine was administered for the last two groups between days 8 and 20 of gestation. On day 21 of gestation, the pup rats were delivered by cesarean section. The levels of IGF-I, IGF-II and IGFBP3 in the brains of pup rats were measured by enzyme-linked immunoadsordent assay (ELISA) and the expression of IGF-I mRNA was detected by fluorescence quantitative PCR (FQ-PCR). RESULTS: The levels of IGF-I, IGF-II and IGF-I mRNA expression in the Model group were significantly lower than in the Control group, with the IGF-I levels of 0.789 +/- 0.062 ng/mg vs 0.947 +/- 0.042 ng/mg, the IGF-II levels of 0.270 +/- 0.020 ng/mg vs 0.374 +/- 0.015 ng/mg and the IGF-I mRNA expression of (13.12 +/- 1.39) x 10(4) cps/mug RNA vs (21.28 +/- 3.54) x 10(4) cps/mug RNA ($P < 0.01$). In contrast, the IGFBP3 levels in the Model group were significantly higher than in the Control group (0.253 +/- 0.011 ng/mg vs 0.089 +/- 0.015 ng/mg; $P < 0.01$). Low or high dose L-arginine treatment increased significantly the IGF-I levels from 0.789 +/- 0.062 ng/mg (Model group) to 0.937 +/- 0.067 ng/mg (low dose group) or 0.858 +/- 0.077 ng/mg (high dose group), the IGF-II levels from 0.270 +/- 0.020 ng/mg (Model group) to 0.318 +/- 0.018 ng/mg (low dose group) or 0.354 +/- 0.021 ng/mg (high dose group) and the IGF-I mRNA expression from (13.12 +/- 1.39) x 10(4) cps/mug RNA (Model group) to (19.24 +/- 2.48) x 10(4) cps/mug RNA (low dose group) or (17.35 +/- 2.30) x 10(4) cps/mug RNA (high dose group) ($P < 0.01$). The IGFBP3 levels were significantly reduced after low or high dose L-arginine treatment (0.132 +/- 0.006 ng/mg or 0.146 +/- 0.009 ng/mg) compared with those of the Model group (0.253 +/- 0.011 ng/mg) ($P < 0.01$). CONCLUSIONS: L-arginine can increase

the levels of IGF-I and IGF-II and the IGF-I mRNA expression, and decrease the IGFBP3 level in the brain of rats with IUGR induced by passive smoking, thereby offering protective effects against IUGR.

L3 ANSWER 9 OF 49 MEDLINE on STN
ACCESSION NUMBER: 2006600064 MEDLINE
DOCUMENT NUMBER: PubMed ID: 16920374
TITLE: Influence of a single course of antenatal betamethasone on the maternal-fetal insulin-IGF-GH axis in singleton pregnancies.
AUTHOR: Ahmad Irfan; Beharry Kay D A; Valencia Arwin M; Cho Steve; Guajardo Leonel; Nageotte Michael P; Modanlou Houchang D
CORPORATE SOURCE: Division of Neonatal-Perinatal Medicine, Department of Pediatrics, University of California Irvine, Orange, CA 92868, USA.
SOURCE: Growth hormone & IGF research : official journal of the Growth Hormone Research Society and the International IGF Research Society, (2006 Aug) Vol. 16, No. 4, pp. 267-75. Electronic Publication: 2006-08-22. Journal code: 9814320. ISSN: 1096-6374.
PUB. COUNTRY: Scotland: United Kingdom
DOCUMENT TYPE: (CONTROLLED CLINICAL TRIAL) Journal; Article; (JOURNAL ARTICLE) (CLINICAL TRIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200611
ENTRY DATE: Entered STN: 13 Oct 2006 Last Updated on STN: 15 Nov 2006 Entered Medline: 14 Nov 2006

AB OBJECTIVE: We examined the hypothesis that a single course of antenatal betamethasone influences the maternal-fetal insulin-IGF-GH axis. DESIGN: A prospective, observational, pilot study consisting of four groups of pregnant women: (I) received betamethasone and delivered <2 weeks post treatment; (II) received betamethasone and delivered >2 weeks post treatment; (III) untreated women who delivered <37 weeks (preterm controls); (IV) untreated women who delivered >37 weeks (term controls). Maternal and mixed umbilical cord blood was collected at delivery and analyzed for insulin, glucose, IGF-I, IGF-II, IGFBP-1, IGFBP-3, GH, and GHBP. RESULTS: Betamethasone increased maternal insulin, glucose and IGF-I levels without affecting IGFBPs. In the fetal compartment, betamethasone treatment was associated with a delayed suppressive effect on GH and a sustained suppressive effect on IGF-II levels. There were no differences in infant size or neonatal morbidities between patients who delivered <2 weeks or >2 weeks post betamethasone treatment. In Group IV, birth weight correlated positively with cord IGF-I levels ($r^2=0.41$, $p=0.0098$) and negatively with cord IGFBP-1 levels ($r^2=0.51$, $p=0.0039$), and ponderal index correlated negatively with cord IGFBP-1 levels ($r^2=0.27$, $p<0.05$). CONCLUSIONS: A single course of antenatal betamethasone influences the maternal-fetal insulin-IGF-GH axis, particularly fetal IGF-II levels, without measurable anthropometric changes at birth. Whether these effects have implications beyond the neonatal period remains to be determined.

L3 ANSWER 10 OF 49 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:1240740 CAPLUS
DOCUMENT NUMBER: 144:4118
TITLE: Genes showing changes in expression in developing and aging in mouse muscle for use in diagnosis and treatment of disease
INVENTOR(S): Kopchick, John J.; Coschigano, Karen T.; Boyce, Keith S.; Kriete, Andres

PATENT ASSIGNEE(S): Ohio University, USA; Icoria, Inc.
SOURCE: PCT Int. Appl., 440 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005110460	A2	20051124	WO 2005-US14441	20050428
WO 2005110460	A3	20060413		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2004-566068P P 20040429
US 2004-577930P P 20040609

AB Mouse genes that show changes in levels of expression in muscle are identified. These genes, and their human equivalent, may be useful as targets in the control of aging and in the treatment of diseases associated with accelerated aging (no data.). The human mols. may also be used as markers of biol. aging.

L3 ANSWER 11 OF 49 MEDLINE on STN DUPLICATE 5
ACCESSION NUMBER: 2005366723 MEDLINE
DOCUMENT NUMBER: PubMed ID: 16024700
TITLE: Effects of L-carnitine on fetal growth and the IGF system in pigs.
AUTHOR: Waylan A T; Kayser J P; Gnad D P; Higgins J J; Starkey J D; Sissom E K; Woodworth J C; Johnson B J
CORPORATE SOURCE: Department of Animal Sciences and Industry, College of Veterinary Medicine, Kansas State University, Manhattan, 66506, USA.
SOURCE: Journal of animal science, (2005 Aug) Vol. 83, No. 8, pp. 1824-31.
Journal code: 8003002. E-ISSN: 1525-3163.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(RANDOMIZED CONTROLLED TRIAL)
(CLINICAL TRIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200606
ENTRY DATE: Entered STN: 19 Jul 2005
Last Updated on STN: 23 Jun 2006
Entered Medline: 22 Jun 2006

AB The effects of L-carnitine on porcine fetal growth traits and the IGF system were determined. Fourth-parity sows were fed a gestation diet with either a 50-g top dress containing 0 (control, n = 6) or 100 mg of L-carnitine (n = 6). At midgestation, fetuses were removed for growth measurements, and porcine embryonic myoblasts (PEM) were isolated from semitendinosus. Real-time quantitative PCR was used to measure growth factor messenger RNA (mRNA) levels in the uterus, placenta, muscle, hepatic tissue, and cultured PEM. A treatment x day interaction (P = 0.02) was observed for maternal circulating total

carnitine. Sows fed L-carnitine had a greater (P = 0.01) concentration of total carnitine at d 57 than control sows. Circulating IGF-I was not affected (P = 0.55) by treatment. Supplementing sows with L-carnitine resulted in larger (P = 0.02) litters (15.5 vs. 10.8 fetuses) without affecting litter weight (P = 0.07; 1,449.6 vs. 989.4 g) or individual fetal weight (P = 0.88) compared with controls. No treatment effect was found for muscle IGF-I (P = 0.36), IGF-II (P = 0.51), IGFBP-3 (P = 0.70), or IGFBP-5 (P = 0.51) mRNA abundance. The abundance of IGF-I (P = 0.72), IGF-II (P = 0.34), and IGFBP-3 (P = 0.99) in hepatic tissue was not influenced by treatment. Uterine IGF-I (P = 0.46), IGF-II (P = 0.40), IGFBP-3 (P = 0.29), and IGFBP-5 (P = 0.35) mRNA abundance did not differ between treatments. Placental IGF-I (P = 0.30), IGF-II (P = 0.18), IGFBP-3 (P = 0.94), and IGFBP-5 (P = 0.42) mRNA abundance did not differ between treatments. There was an effect of side of the uterus for IGF-I (P = 0.04) and IGF-II (P = 0.007) mRNA abundance; IGF-I mRNA abundance was greater in the left uterine horn than in the right uterine horn (0.14 and 0.07 relative units, respectively). Placental IGF-II mRNA abundance was greater (P = 0.007) in the left than in the right uterine horn (483.5 and 219.59, respectively). The abundance of IGFBP-3 was not affected by uterine horns in either uterine (P = 0.66) or placental (P = 0.13) tissue. There was no treatment difference for IGF-I (P = 0.31) or IGFBP-5 (P = 0.13) in PEM. The PEM isolated from sows fed L-carnitine had decreased IGF-II (P = 0.02), IGFBP-3 (P = 0.03), and myogenin (P = 0.04; 61, 59, and 67%, respectively) mRNA abundance compared with controls. These data suggest that L-carnitine supplemented to gestating sows altered the IGF system and may affect fetal growth and development.

L3 ANSWER 12 OF 49 MEDLINE on STN DUPLICATE 6
ACCESSION NUMBER: 2005604676 IN-PROCESS
DOCUMENT NUMBER: PubMed ID: 16126771
TITLE: Posttranslational modifications of decidual IGFBP-1 by steroid hormones in vitro.
AUTHOR: Kabir-Salmani M; Shimizu Y; Sakai K; Iwashita M
CORPORATE SOURCE: Department of Obstetrics and Gynecology, Kyorin University School of Medicine, Mitaka, Tokyo, Japan.. kabirs_m@yahoo.com
SOURCE: Molecular human reproduction, (2005 Sep) Vol. 11, No. 9, pp. 667-71. Electronic Publication: 2005-08-26. Journal code: 9513710. ISSN: 1360-9947.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE) (RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE: English
FILE SEGMENT: NONMEDLINE; IN-PROCESS; NONINDEXED; Priority Journals
ENTRY DATE: Entered STN: 15 Nov 2005
Last Updated on STN: 13 Dec 2006

AB Insulin-like growth factor binding protein-1 (IGFBP-1) appears to regulate insulin-like growth factors (IGFs; IGF-I and IGF-II) biological activity within the local environment of human placenta by modulating IGFs interaction with their receptors. Considering that posttranslational modifications of IGFBP-1 such as phosphorylation and proteolysis affect its affinity for IGFs, this study was undertaken to identify the role of estrogen and progesterone in this regard. The conditioned media of steroid hormone-treated decidual cells were evaluated using different approaches using sodium dodecyl sulphate-polyacrylamide gel electrophoresis (SDS-PAGE) and non-denaturing PAGE following immunoblotting as well as zymographys that contained gelatin and IGFBP-1 as substrates. Our results demonstrated that medroxy progesterone acetate (MPA) treatment increased both phosphorylated and non-phosphorylated decidual-secreted IGFBP-1, whereas 17beta-estradiol

(E2) treatment attenuated its phosphorylated forms. Furthermore, the results of zymography revealed that steroid hormones regulated the activity of decidual-secreted matrix metalloproteinases (MMP)-2 and -9, in which E2 treatment up-regulated the MMP-9 activity. Finally, it was demonstrated in our study that decidual-secreted MMP-9 was capable of degrading human amniotic fluid-derived IGFBP-1. In conclusion, our data implicate steroid hormones in the control of IGF system activities at the embryo-maternal interface, at least in part, through their effects on the post-translation changes of decidual-secreted IGFBP-1 such as its phosphorylation and/or proteolysis.

L3 ANSWER 13 OF 49 MEDLINE on STN DUPLICATE 7
ACCESSION NUMBER: 2005511706 MEDLINE
DOCUMENT NUMBER: PubMed ID: 16183872
TITLE: Endocrine disruption of uterine insulin-like growth factor expression in the pregnant gilt.
AUTHOR: Ashworth M D; Ross J W; Stein D R; Allen D T; Spicer L J; Geisert R D
CORPORATE SOURCE: Department of Animal Science, Oklahoma Agricultural Experiment Station, Animal Science Building, Oklahoma State University, Stillwater, Oklahoma 74078, USA.
SOURCE: Reproduction (Cambridge, England), (2005 Oct) Vol. 130, No. 4, pp. 545-51.
Journal code: 100966036. ISSN: 1470-1626.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200603
ENTRY DATE: Entered STN: 27 Sep 2005
Last Updated on STN: 3 Mar 2006
Entered Medline: 2 Mar 2006

AB Early exposure of pregnant gilts to oestrogen, prior to the normal period of porcine conceptus oestrogen secretion, disrupts the uterine environment resulting in complete embryonic mortality during the period of placental attachment to the uterine surface. The current study evaluates the uterine insulin-like growth factor (IGF) system following endocrine disruption of early pregnancy in gilts through exposure to exogenous oestrogen on Days 9 and 10 of gestation. Endometrial IGF gene and protein expression, IGF-I receptor (IGF-IR) gene expression, and uterine lumenal content of IGF binding proteins (IGFBPs) were evaluated in control and oestrogen-treated gilts on Days 10, 12, 13, 15 and 17 of gestation. Oestrogen treatment altered endometrial IGF-I and IGF-IR gene expression on Days 12 and 13 of gestation. Uterine content of IGF-I and IGF-II in control gilts was greatest on Days 10, 12, and 13 followed by a four- to sixfold decrease on Day 15 of gestation. Oestrogen treatment caused a premature proteolysis of IGFBPs within the pregnant pig uterus on Day 10 of gestation, and an earlier decline in uterine lumenal IGF-I content. Results demonstrate that early exposure of pregnant gilts to oestrogen causes premature loss of uterine IGFs during the period of conceptus elongation. Timing for the release of uterine IGFs during early porcine conceptus development may play an important function in the ability of the conceptus to attach and survive during the establishment of pregnancy.

L3 ANSWER 14 OF 49 MEDLINE on STN DUPLICATE 8
ACCESSION NUMBER: 2005483477 MEDLINE
DOCUMENT NUMBER: PubMed ID: 16153497
TITLE: Exogenous somatotropin alters IGF axis in porcine endometrium and placenta.
AUTHOR: Freese L G; Rehfeldt C; Fuerbass R; Kuhn G; Okamura C S; Ender K; Grant A L; Gerrard D E
CORPORATE SOURCE: Department of Animal Sciences, Purdue University, West Lafayette, IN 47907, USA.

SOURCE: Domestic animal endocrinology, (2005 Oct) Vol. 29, No. 3, pp. 457-75. Electronic Publication: 2005-03-07. Journal code: 8505191. ISSN: 0739-7240.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200512
ENTRY DATE: Entered STN: 13 Sep 2005
Last Updated on STN: 15 Dec 2005
Entered Medline: 8 Dec 2005

AB The aim of this study was to examine whether exogenous somatotropin (ST) can alter the insulin-like growth factor (IGF) axis in the porcine epitheliochorial placenta. Crossbred gilts were injected either 6 mg of recombinant porcine ST or vehicle from days 10 to 27 after artificial insemination (term day 116). Control and ST-treated gilts were euthanized on day 28 (8 control/5 treated), day 37 (4 control/6 treated), and day 62 (4 control/6 treated) of gestation. Endometrium and placental tissue samples were collected and subjected to mRNA analyses. In control gilts, somatotropin receptor (STR) and IGF-I mRNA abundance in the endometrium decreased with gestation. Conversely, the amounts of IGF-II mRNA and of IGF binding protein (BP)-2 and -3 mRNA, which were analyzed in endometrium and placental chorion, increased with gestation. The endometrium contained less IGF-II mRNA but more IGFBP-2 and-3 mRNA than the placental chorion. In response to pST treatment, the amounts of endometrial STR and IGF-I mRNA were lower at days 28 and 37, but higher at day 62 of gestation. The content of IGF-II mRNA was higher in the endometrium of pST-treated than control gilts on day 37. The amount of IGFBP-2 mRNA was increased on day 37 in endometrium and placenta of pST-treated gilts, whereas no changes in IGFBP-3 mRNA were observed. The IGF -II/IGFBP-2 ratio was higher in the placenta in response to pST on day 28 of gestation. Results show that pST treatment of pregnant gilts during early gestation alters IGF axis in maternal and fetal placental tissues and suggest pST may exert an effect on fetal growth by altering the relative amount of IGFBPs and IGFs at the fetal-maternal interface.

L3 ANSWER 15 OF 49 MEDLINE on STN
ACCESSION NUMBER: 2005254654 MEDLINE
DOCUMENT NUMBER: PubMed ID: 15749784
TITLE: HCG increases trophoblast migration in vitro via the insulin-like growth factor-II/mannose-6 phosphate receptor.
AUTHOR: Zygmunt M; McKinnon T; Herr F; Lala P K; Han V K M
CORPORATE SOURCE: MRC Group in Fetal and Neonatal Health and Development, The Lawson Research Institute and The Child Health Research Institute, London, Ontario, Canada.. marek.t.zygmunt@gyn.med.uni-giessen.de
SOURCE: Molecular human reproduction, (2005 Apr) Vol. 11, No. 4, pp. 261-7. Electronic Publication: 2005-03-04. Journal code: 9513710. ISSN: 1360-9947.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200510
ENTRY DATE: Entered STN: 18 May 2005
Last Updated on STN: 6 Oct 2005
Entered Medline: 5 Oct 2005

AB We have previously shown that both HCG and insulin-like growth factor-II (IGF-II) stimulate trophoblastic invasion. Furthermore, the invasion-promoting function of IGF-II resulted from IGF-II mannose 6-phosphate receptor (IGF

-II/M6PR) activation. Since HCG and IGF-II did not have an additive effect on cell migration of extravillous trophoblast (EVT) cell line, HTR-8 SVneo, we hypothesized that HCG actions are mediated via alterations in the expression and/or function of IGF-II axis. HCG treatment (50-50,000 mU/ml) of the HTR-8/SVneo cells did not alter the expression of either insulin-like growth factor-I or IGF-II mRNA or peptide synthesis, but caused (i) an increase in the (125)I-IGF-II binding to EVT cells, and (ii) an increase in the externalization rate of the IGF-II binding sites without affecting their internalization. This effect was due to the increase in the number of IGF-II binding sites in the plasma membrane without any change in the IGF-II binding affinity. Although HCG did not influence the abundance of IGF-II/M6PR mRNA or protein, anti-IGF-II/M6PR antibody decreased HCG-induced migration of EVT, supporting the hypothesis that HCG might stimulate EVT migration by increasing IGF-II binding to the plasma membrane and subsequently by increasing the IGF-II effect probably mediated via the IGF-II/M6PR.

L3 ANSWER 16 OF 49 MEDLINE on STN DUPLICATE 9
ACCESSION NUMBER: 2003038925 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12548223
TITLE: Relaxin causes proliferation of human amniotic epithelium by stimulation of insulin-like growth factor-II.
AUTHOR: Millar Lynnae K; Reiny Roxanne; Yamamoto Sandra Y; Okazaki Kristie; Webster Lisa; Bryant-Greenwood Gillian D
CORPORATE SOURCE: Pacific Biomedical Research Center and the Divisions of Cell and Molecular Biology and Obstetrics and Gynecology, University of Hawaii, Honolulu, HI 96822, USA..
LynnaeM@apiolani.org
CONTRACT NUMBER: G12 RR003061-20 (NCRR)
HD-24314 (NICHD)
P20 RR011091-11 (NCRR)
R01 HD024314-15 (NICHD)
RR-11091 (NCRR)
RR1A1-03061 (NCRR)
U54 RR014607-05 (NCRR)
SOURCE: American journal of obstetrics and gynecology, (2003 Jan) Vol. 188, No. 1, pp. 234-41.
Journal code: 0370476. ISSN: 0002-9378.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 200302
ENTRY DATE: Entered STN: 28 Jan 2003
Last Updated on STN: 21 Feb 2003
Entered Medline: 20 Feb 2003

AB OBJECTIVE: The study was conducted to determine whether relaxin has a proliferative effect on amniotic epithelial cells and to show that this effect is caused by its stimulation of the insulin-like growth factor-II (IGF-II) gene. STUDY DESIGN: Immunolocalization and Northern analysis were used to confirm the expression of IGF-II by the fetal cells in the membranes. Human amniotic epithelial (WISH) cells were treated with doses of IGF-II or human relaxin and their proliferative effects measured. The mechanism of the effect of relaxin on cellular proliferation was studied with the use of an IGF-II-blocking antibody and Northern analysis for IGF-II gene expression after treatment with relaxin. An in vivo correlate was sought by quantitation of relaxin gene expression in 10 fetal membranes from women with normally grown and large for gestational age infants. RESULTS: The amniotic epithelial and

cytotrophoblast cells of the fetal membranes expressed IGF-II, as did the amniotic epithelial-like (WISH) cell line. Treatment of WISH cells with IGF-II or relaxin caused a significant (P <.03) and dose-related increase in WISH cell proliferation over 5 days. The concurrent treatment with a blocking antibody to IGF-II significantly decreased the proliferative response to IGF-II (P <.002) and relaxin (P <.002). Treatment with relaxin caused a significant increase (P <.003) in the transcription of IGF-II in 24 hours. In fetal membranes, the levels of relaxin gene expression correlated with fetal membrane surface area (r = 0.76) and was significantly greater (P <.008) in the membranes from macrosomic infants (4020-4729 g) compared with those normally grown (2855-3830 g). CONCLUSION: IGF-II and relaxin both caused the proliferation of WISH cells. Concurrent treatment with an IGF-II-blocking antibody abrogated the proliferative effects of both hormones. Relaxin increased the transcription of IGF-II, and its expression levels in the fetal membranes correlated with the membrane surface area as well as neonatal birth weight. These data suggest that relaxin is a growth factor for the fetal membranes.

L3 ANSWER 17 OF 49 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2002:971500 CAPLUS
DOCUMENT NUMBER: 138:232144
TITLE: Characterization of morphological and cytoskeletal changes in trophoblast cells induced by insulin-like growth factor-I
AUTHOR(S): Kabir-Salmani, Maryam; Shiokawa, Shigetatsu; Akimoto, Yoshihiro; Hasan-Nejad, Habib; Sakai, Keiji; Nagamatsu, Shinya; Sakai, Ken; Nakamura, Yukio; Hosseini, Ahmad; Iwashita, Mitsutoshi
CORPORATE SOURCE: Departments of Obstetrics and Gynecology, Kyorin University School of Medicine, Tokyo, 181-8611, Japan
SOURCE: Journal of Clinical Endocrinology and Metabolism (2002), 87(12), 5751-5759
CODEN: JCEMAZ; ISSN: 0021-972X
PUBLISHER: Endocrine Society
DOCUMENT TYPE: Journal
LANGUAGE: English

AB IGF-I and IGF-II were appeared to play major roles in the adhesive and migratory events that are considered to be crucial in the implantation process. The purpose of this study was to determine the effects of IGF-I on trophoblast adhesion to extracellular matrix. Trophoblast cells obtained from early gestation at artificial abortion were incubated with the indicated doses of IGF-I at the indicated times. Trophoblast cells were treated with IGF-I in the presence or absence of RGD peptide and an antibody against α-subunit of IGF-I receptor (αIR3). Morphometric and morphol. changes were studied using light and electron microscopy. Furthermore, vinculin, actin stress fibers, phosphorylated focal adhesion kinase (FAK), phosphotyrosine, and paxillin were immunolocalized in trophoblast cells after IGF-I treatment in the presence or absence of αIR3. Immunopptn. and anti-phosphotyrosine immunoblotting were carried out to detect the phosphorylated FAK and phosphorylated paxillin contents of the IGF-I-treated and untreated trophoblast cells. The results showed that IGF-I promoted trophoblast adhesion to fibronectin substrate in a time- and dose-dependent manner, and addition of RGD peptide and αIR3 monoclonal antibody abolished the effects of IGF-I in these cells. Morphol. studies exhibited an increase in the lamellipodia formation upon IGF-I treatment, and confocal images of immunofluorescent staining revealed localization of phosphorylated FAK, paxillin, and vinculin at focal adhesions as well as redistribution of actin microfilaments and formation of actin stress fibers inside the cell.

Western blotting, using antiphosphotyrosine demonstrated proteins with mol. masses of 125 kDa (FAK) and 68 kDa (paxillin) present in the IGF-I-treated cells, which were lacking in the control groups. In conclusion, these findings suggest that IGF-I can stimulate lamellipodia formation and promote adhesion of trophoblast cells to extracellular matrix by activating their adhesion mols. that must be activated within the implantation window.

REFERENCE COUNT: 42 THERE ARE 42 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 18 OF 49 MEDLINE on STN
ACCESSION NUMBER: 2002301945 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12021036
TITLE: Clinical, hormonal, and hematologic characteristics of bovine calves derived from nuclei from somatic cells.
AUTHOR: Chavatte-Palmer P; Heyman Y; Richard C; Monget P; LeBourhis D; Kann G; Chilliard Y; Vignon X; Renard J P
CORPORATE SOURCE: Biologie du Developpement et Biotechnologies, Unite Mixte de Recherche Institut National de la Recherche Agronomique/Ecole Nationale Veterinaire d'Alfort, Domaine de Vilvert, 78352 Jouy en Josas cedex, France.. chavatte@jouy.inra.fr
SOURCE: Biology of reproduction, (2002 Jun) Vol. 66, No. 6, pp. 1596-603.
Journal code: 0207224. ISSN: 0006-3363.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200301
ENTRY DATE: Entered STN: 5 Jun 2002
Last Updated on STN: 15 Jan 2003
Entered Medline: 14 Jan 2003

AB Although healthy animals are born after nuclear transfer with somatic cells nuclei, the success of this procedure is generally poor (2%-10%) with high perinatal losses. Apparently normal surviving animals may have undiagnosed pathologies that could develop later in life. The gross pathology of 16 abnormal bovine fetuses produced by nuclear transfer (NT) and the clinical, endocrinologic (insulin-like growth factors I and II [IGF-I and IGF-II], IGF binding proteins, post-ACTH stimulation cortisol, leptin, glucose, and insulin levels), and biochemical characteristics of a group of 21 apparently normal cloned calves were compared with those of in vitro-produced (IVP) controls and controls resulting from artificial insemination. Oocytes used for NT or IVP were matured in vitro. NT to enucleated oocytes was performed using cultured adult or fetal skin cells. After culture, Day 7, grade 1-2 embryos were transferred (one per recipient). All placentas and fetuses from clones undergoing an abnormal pregnancy showed some degree of edema due to hydrops. Mean placentome number was lower and mean placentome weight was higher in clones than in controls (69.9 +/- 9.2 placentomes with a mean weight of 144.3 +/- 21.4 g in clones vs. 99 and 137 placentomes with a mean individual weight of 34.8 and 32.4 g in two IVP controls). Erythrocyte mean cell volume was higher at birth ($P < 0.01$), and body temperature and plasma leptin concentrations were higher and T4 levels were lower during the first 50 days and the first week ($P < 0.05$), respectively, in clones. Plasma IGF-II concentrations were higher at birth and lower at Day 15 in clones ($P < 0.05$). Therefore, apparently healthy cloned calves cannot be considered as physiologically normal animals until at least 50 days of age.

L3 ANSWER 19 OF 49 MEDLINE on STN DUPLICATE 10
ACCESSION NUMBER: 2002641541 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12400877
TITLE: Immune stimulation in urethane-exposed pregnant mice

increases expression level of spleen leukocyte genes for TGFbeta3 GM-CSF and other cytokines that may play a role in reduced chemical-induced birth defects.

AUTHOR: Sharova L V; Gogal R M Jr; Sharov A A; Chrisman M V; Holladay S D

CORPORATE SOURCE: Department of Biomedical Sciences and Pathobiology, Virginia-Maryland Regional College of Veterinary Medicine, Virginia Polytechnic Institute and State University, Blacksburg 24061-0442, USA.

SOURCE: International immunopharmacology, (2002 Sep) Vol. 2, No. 10, pp. 1477-89.
Journal code: 100965259. ISSN: 1567-5769.

PUB. COUNTRY: Netherlands

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 200304

ENTRY DATE: Entered STN: 29 Oct 2002
Last Updated on STN: 1 May 2003
Entered Medline: 30 Apr 2003

AB For unknown reasons, activation of the maternal immune system in mice reduces morphologic defects caused by diverse teratogenic agents. Such immune stimulation of the maternal animal has been correlated with altered cytokine mRNA transcripts in the placenta (e.g., TGFbeta2) as well as in fetal target tissues of the teratogen (e.g., TNFalpha in fetal heads of cyclophosphamide-exposed pregnant mice). The teratogen urethane was reported to down-regulate cell cycle and apoptotic regulatory genes in fetal mouse heads that displayed cleft palate, an effect that was also reversed by maternal immune stimulation. The molecular mediators of the above phenomena have not been identified, however proteins synthesized and released by activated maternal immune cells have been suggested. The present studies therefore evaluated the effects of maternal immune stimulation in urethane-exposed mice on thymus and spleen leukocyte populations, in an attempt to identify events that may correlate with protection against birth defects. Immune stimulation did not change the hypocellularity of the thymus nor the altered T cell differentiation caused by urethane. A limited and transient increase in splenic leukocyte number, including increased T and B lymphocytes and macrophages, was caused by immune stimulation and was not felt to play a significant role in reduced morphologic defects. Urethane treatment caused down-regulated expression of numerous genes involved in cell-cycle control, while maternal immune stimulation caused comparative up-regulation of many of these genes. Coordinate shifts in gene expression by treatment were evaluated using principal component analysis, which identified several growth factor genes that were differentially expressed in mice receiving urethane alone as compared to urethane plus immune stimulation. Up-regulated expression of TGFbeta3 and GM-CSF genes, in particular, was observed in leukocytes of urethane-exposed mice receiving immunostimulation. Interestingly, the cytokine products of these two genes were recently suggested as growth factors that may be related to reduction of fetal defects caused by teratogens. Genes for growth factors IGF-I, IGF-II and IL-2 were also identified as differentially expressed in urethane vs. urethane+immune stimulation mice, suggesting that these proteins should be considered for a potential contributing effect to reduced birth defects caused by immunostimulation.

L3 ANSWER 20 OF 49 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2001:850890 CAPLUS

DOCUMENT NUMBER: 136:1666

TITLE: cDNA and polypeptide sequences for human insulin-like growth factor binding protein 3 receptor (IGF-BP-3R), an IGF-independent IGFBP-3 interacting protein, and their diagnostic and therapeutic uses

INVENTOR(S): Oh, Youngman; Rosenfeld, Ron; Ingermann, Angela Ranae
PATENT ASSIGNEE(S): Oregon Health & Sciences University, USA
SOURCE: PCT Int. Appl., 109 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001087238	A2	20011122	WO 2001-US16437	20010517
WO 2001087238	A3	20020606		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2410056	A1	20011122	CA 2001-2410056	20010517
AU 2001064769	A5	20011126	AU 2001-64769	20010517
EP 1290162	A2	20030312	EP 2001-939229	20010517
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
US 2004072285	A1	20040415	US 2003-276491	20030220
PRIORITY APPLN. INFO.:			US 2000-204949P P	20000517
			WO 2001-US16437 W	20010517

AB There is disclosed an isolated cDNA sequence (SEQ ID NO:1), clone 4.33, encoding a polypeptide and comprising a coding region (SEQ ID NO:2) of the sequence described in SEQ ID NO:1, or a sequence having at least 90% homol. with the coding region of SEQ ID NO:1. The clone 4.33 polypeptide functions as a specific cell-surface receptor for IGF-BP-3 (insulin-like growth factor binding protein 3), and undergoes nuclear translocation in combination with IGF-BP-3. IGF-BP-3 and IGF-BP-3R (insulin-like growth factor binding protein 3 receptor P4.33) cooperatively suppress DNA synthesis and cell growth, and induce caspase activation and apoptosis in cancer cells, indicating that clone 4.33 is an important mediator of IGF-independent growth inhibitory actions of IGF-BP-3. The P4.33:IGFBP-3 system of the present invention can be used, inter alia, in screening and diagnostic assays, and for therapeutic methods for cancer treatment and tumor suppression. CDNA clone 4.33 is expressed in multiple human tissues and is differentially expressed in normal vs. cancerous human cell lines. There is a significant decrease in endogenous expression of clone 4.33 in PC-3 prostate cancer cells. Exptl. results from overexpression of IGF-BP-3R in cancer cell lines suggest that it represents a novel mammalian cell death receptor.

L3 ANSWER 21 OF 49 MEDLINE on STN DUPLICATE 11
ACCESSION NUMBER: 2001545242 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11566745
TITLE: Developmental regulation of placental insulin-like growth factor (IGF)-II and IGF-binding protein-1 and -2 messenger RNA expression during primate pregnancy.
AUTHOR: Zollers W G Jr; Babischkin J S; Pepe G J; Albrecht E D
CORPORATE SOURCE: Department of Obstetrics, Gynecology and Reproductive Sciences, University of Maryland School of Medicine, Baltimore, Maryland 21201, USA.
CONTRACT NUMBER: HD-13294 (NICHD)
SOURCE: Biology of reproduction, (2001 Oct) Vol. 65, No. 4, pp. 1208-14.

Journal code: 0207224. ISSN: 0006-3363.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200112
ENTRY DATE: Entered STN: 11 Oct 2001
Last Updated on STN: 22 Jan 2002
Entered Medline: 5 Dec 2001

AB The present study was conducted to determine the developmental expression of placental insulin-like growth factor (IGF)-II, IGF-binding protein (IGFBP)-1 and -2, and IGF-II receptor mRNA expression during baboon pregnancy and whether estrogen, the levels of which increase with advancing pregnancy, regulates placental trophoblast IGF-II mRNA expression. Levels of the IGF-II 6.1-kilobase (kb) and 4.9-kb mRNA transcripts determined by Northern blot analysis progressively increased three- to fourfold in placental syncytiotrophoblast and whole-villous tissue between early (Day 60), mid (Day 100), and late (Day 170) baboon gestation (term = 184 days). In contrast, syncytiotrophoblast IGFBP-1 and -2 mRNA levels decreased, and IGF-II receptor mRNA expression remained relatively constant, with advancing baboon pregnancy. Placental cytotrophoblast IGF-II mRNA levels determined by competitive reverse transcription-polymerase chain reaction on Day 54 of gestation were increased ($P < 0.05$) almost twofold at 18 h after acute administration of estradiol to baboons, whereas long-term estrogen treatment had no effect. We propose that these changes in trophoblast IGF expression would provide a mechanism for enhancing net bioavailability and bioreactivity of IGF-II locally to promote the growth and development of the placenta and, consequently, of the fetus during primate pregnancy.

L3 ANSWER 22 OF 49 MEDLINE on STN DUPLICATE 12
ACCESSION NUMBER: 2002234548 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11914027
TITLE: Maternal nutrition affects the ability of treatment with IGF-I and IGF-II to increase growth of the placenta and fetus, in guinea pigs.
AUTHOR: Sohlstrom A; Fernberg P; Owens J A; Owens P C
CORPORATE SOURCE: Department of Physiology and Pharmacology, Karolinska Institutet, S-171 77 Stockholm, Sweden.. annica.sohlstrom@ibk.liu.se
SOURCE: Growth hormone & IGF research : official journal of the Growth Hormone Research Society and the International IGF Research Society, (2001 Dec) Vol. 11, No. 6, pp. 392-8. Journal code: 9814320. ISSN: 1096-6374.
PUB. COUNTRY: Scotland: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200206
ENTRY DATE: Entered STN: 26 Apr 2002
Last Updated on STN: 4 Jun 2002
Entered Medline: 3 Jun 2002

AB The aim of this study was to investigate how administration of IGF-I and IGF-II, during early to mid pregnancy, affects maternal growth and body composition as well as fetal and placental growth, in ad libitum fed, and in moderately, chronically food restricted guinea pigs. From day 20 of gestation, mothers (3-4 months old) were infused with IGF-I, IGF-II (565 microg/day) or vehicle for 17 days and then killed on day 40 of gestation. Maternal organ weights, fetal and placental weights were assessed. Treatment with IGFs did not alter body weight gain and had small

effects on body composition in the mothers. Both IGF-I and IGF-II increased fetal and placental weights in ad libitum fed dams and IGF-I increased placental weight in food restricted dams. In conclusion, treatment with IGF-I during the first half of pregnancy stimulates placental growth in both ad libitum fed and food restricted guinea pigs without affecting maternal growth while fetal growth is stimulated by IGF treatment only in ad libitum fed animals.

L3 ANSWER 23 OF 49 MEDLINE on STN DUPLICATE 13
ACCESSION NUMBER: 2000325235 MEDLINE
DOCUMENT NUMBER: PubMed ID: 10864806
TITLE: Effect of a high maternal dietary intake during mid-gestation on components of the utero-placental insulin-like growth factor (IGF) system in adolescent sheep with retarded placental development.
AUTHOR: Gadd T S; Aitken R P; Wallace J M; Wathes D C
CORPORATE SOURCE: Department of Veterinary Basic Sciences, The Royal Veterinary College, Boltons Park, Hawkshead Road, Potters Bar, Hertfordshire EN6 1NB, UK.
SOURCE: Journal of reproduction and fertility, (2000 Mar) Vol. 118, No. 2, pp. 407-16.
Journal code: 0376367. ISSN: 0022-4251.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200007
ENTRY DATE: Entered STN: 28 Jul 2000
Last Updated on STN: 28 Jul 2000
Entered Medline: 14 Jul 2000

AB The aim of the present study was to investigate the effects of administering a high plane diet during early to mid-gestation on the uterine and placental insulin-like growth factor (IGF) system and on systemic IGF-I concentrations in pregnant adolescent ewes with restricted placental growth. Embryos recovered from superovulated ewes inseminated by a single sire were transferred in singleton to the uterus of adolescent recipients. After transfer ewes were offered a high (H) or moderate (M) amount of a complete diet calculated to promote rapid or normal maternal growth rates, respectively. Five ewes from each group were switched from either M to H or H to M diets at day 52 of gestation. Maternal and fetal blood samples and placental tissues were collected from all animals at day 104. Ewes on the high plane diet from mid-gestation (HH, MH groups) had restricted placental mass ($P < 0.01$) and tended to have smaller fetuses. This was associated with increased maternal plasma IGF-I concentrations ($P < 0.001$). The pattern of expression of components of the IGF system in the uterus and placenta was studied by in situ hybridization. IGF-I mRNA concentrations were below the limit of detection. IGF-II mRNA expression was high in the fetal mesoderm and present in maternal stroma, but was not influenced by nutritional treatment. In contrast, IGF binding protein 1 (IGFBP-1) mRNA expression was higher ($P < 0.05$) and IGFBP-3 mRNA expression was lower ($P < 0.05$) in the endometrial glands of ewes in HH and MH groups. In the fetal trophoblast, IGFBP-3 mRNA expression was higher in the MH group. Type 1 IGF receptor expression was increased ($P < 0.01$) in the luminal epithelium of the HM group and IGFBP-2 mRNA expression was highest in the placentome capsule of ewes in the HH group. Together, these results indicate that reprogramming of the uterine and placental IGF axis by maternal nutrition could contribute to placental growth retardation in growing adolescent sheep.

L3 ANSWER 24 OF 49 EMBASE

reserved on STN

ACCESSION NUMBER: 2000362322 EMBASE
TITLE: Effects of maternal captopril treatment on growth, blood glucose and plasma insulin in the fetal spontaneously hypertensive rat.
AUTHOR: Lewis R.M.; Vickers M.H.; Batchelor D.C.; Bassett N.S.; Johnston B.M.; Skinner S.J.M.
CORPORATE SOURCE: R.M. Lewis, Department of Clinical Biochemistry, University of Cambridge, Box 232 Addenbrooke's Hospital, Hills Road, Cambridge CB2 2QR, United Kingdom. rml28@cam.ac.uk
SOURCE: Reproduction, Fertility and Development, (2000) Vol. 11, No. 7-8, pp. 403-408.
Refs: 25
ISSN: 1031-3613 CODEN: RFDEEH
COUNTRY: Australia
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 010 Obstetrics and Gynecology
018 Cardiovascular Diseases and Cardiovascular Surgery
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 13 Nov 2000
Last Updated on STN: 13 Nov 2000

AB In the spontaneously hypertensive rat (SHR) fetal growth and metabolism are abnormal. It has been speculated that maternal hypertension may be the cause of these abnormalities. Captopril treatment, which reduces maternal blood pressure, during pregnancy and lactation, is reported to have a beneficial effect postnatally, normalizing the blood pressure of offspring in the SHR. In the present study, the effects of maternal captopril treatment on fetal growth and plasma metabolites were investigated in the fetuses of two rat strains (SHR and Wistar-Kyoto (WKY)), in order to determine whether normalizing maternal blood pressure also normalized abnormalities in fetal growth and metabolism. On fetal Day 20, SHR fetuses were lighter and placentae were heavier than for the corresponding WKY. Captopril had no effect on fetal weight in the SHR, but decreased it in the WKY. There was no effect of captopril on placental weight. Fetal plasma insulin levels were higher in the SHR than in the WKY and were decreased by captopril treatment in both strains. Fetal blood glucose was elevated and fetal blood lactate was decreased in captopril-treated litters from both strains. Captopril had no effect on fetal plasma IGF-1 but fetal plasma IGF-2 levels were lower in the captopril-treated SHR than in the captopril-treated WKY. These findings suggest that maternal captopril treatment decreases insulin secretion in the fetal rat. High levels of fetal plasma insulin suggest that the SHR fetus is insulin resistant. Fetal insulin levels may contribute to the adverse consequences of gestational captopril treatment observed in many species. The differences in the effect of captopril on the two strains suggest that there are underlying endocrine differences in the SHR.

L3 ANSWER 25 OF 49 MEDLINE on STN DUPLICATE 14
ACCESSION NUMBER: 2001064249 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11101275
TITLE: Effects of maternal captopril treatment on growth, blood glucose and plasma insulin in the fetal spontaneously hypertensive rat.
AUTHOR: Lewis R M; Vickers M H; Batchelor D C; Bassett N S; Johnston B M; Skinner S J
CORPORATE SOURCE: Research Centre for Developmental Medicine and Biology, University of Auckland, New Zealand.. rml28@cam.ac.uk
SOURCE: Reproduction, fertility, and development, (1999) Vol. 11, No. 7-8, pp. 403-8.
Journal code: 8907465. ISSN: 1031-3613.

PUB. COUNTRY: Australia
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200012
ENTRY DATE: Entered STN: 22 Mar 2001
Last Updated on STN: 22 Mar 2001
Entered Medline: 22 Dec 2000

AB In the spontaneously hypertensive rat (SHR) fetal growth and metabolism are abnormal. It has been speculated that maternal hypertension may be the cause of these abnormalities. Captopril treatment, which reduces maternal blood pressure, during pregnancy and lactation, is reported to have a beneficial effect postnatally, normalizing the blood pressure of offspring in the SHR. In the present study, the effects of maternal captopril treatment on fetal growth and plasma metabolites were investigated in the fetuses of two rat strains (SHR and Wistar-Kyoto (WKY)), in order to determine whether normalizing maternal blood pressure also normalized abnormalities in fetal growth and metabolism. On fetal Day 20, SHR fetuses were lighter and placentae were heavier than for the corresponding WKY. Captopril had no effect on fetal weight in the SHR, but decreased it in the WKY. There was no effect of captopril on placental weight. Fetal plasma insulin levels were higher in the SHR than in the WKY and were decreased by captopril treatment in both strains. Fetal blood glucose was elevated and fetal blood lactate was decreased in captopril-treated litters from both strains. Captopril had no effect on fetal plasma IGF-1 but fetal plasma IGF-2 levels were lower in the captopril-treated SHR than in the captopril-treated WKY. These findings suggest that maternal captopril treatment decreases insulin secretion in the fetal rat. High levels of fetal plasma insulin suggest that the SHR fetus is insulin resistant. Fetal insulin levels may contribute to the adverse consequences of gestational captopril treatment observed in many species. The differences in the effect of captopril on the two strains suggest that there are underlying endocrine differences in the SHR.

L3 ANSWER 26 OF 49 MEDLINE on STN DUPLICATE 15
ACCESSION NUMBER: 1999091719 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9868179
TITLE: Maternal and fetal insulin-like growth factor system and embryonic survival during pregnancy in rats: interaction between dietary chromium and diabetes.
AUTHOR: Spicer M T; Stoecker B J; Chen T; Spicer L J
CORPORATE SOURCE: Department of Nutritional Sciences, Oklahoma State University, Stillwater, OK 74078, USA.
SOURCE: The Journal of nutrition, (1998 Dec) Vol. 128, No. 12, pp. 2341-7.
Journal code: 0404243. ISSN: 0022-3166.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199901
ENTRY DATE: Entered STN: 9 Feb 1999
Last Updated on STN: 9 Feb 1999
Entered Medline: 27 Jan 1999

AB Chromium (Cr) depletion may exacerbate hyperglycemia and negative outcomes of pregnancy in the streptozotocin (STZ) diabetic pregnant rat model through the regulation of the insulin-like growth factor (IGF) system. To test this hypothesis, 40 female rats, all fed a low Cr diet (i.e., 70 microgram Cr/kg diet) from 21 d of age, were randomly assigned one of four treatments, applied on Day 1 of pregnancy, in a 2 x 2 factorial design: 1) very low Cr diet (40 microgram Cr/kg diet) + citrate buffer injection, 2) very low Cr diet + STZ injection (30 mg STZ/kg body

wt in citrate buffer), 3) adequate Cr diet (2 mg Cr [from added CrK(SO4)2]/kg diet) + citrate buffer injectionand 4) adequate Cr diet + STZ injection. Blood and tissues were collected on Day 20 of pregnancy. Chromium depletion increased (P < 0.05) urinary hydroxyproline excretion, 22-kDa IGF binding protein (IGFBP) concentration and litter size but decreased (P < 0. 05) placental wt, percentage of protein per fetus, and fetal IGF-I and -II concentrations. Chromium had no effect (P > 0.10) on maternal hormones, 32-kDa IGFBP, glucose, or placental and fetal hydroxyproline concentrations. Diabetes decreased (P < 0.05) maternal wt gain, embryonic survival, litter size, mean pup wt and maternal insulin concentrations, increased (P < 0.05) maternal blood glucose, IGF-I concentrations and maternal hydroxyproline excretion but did not affect fetal concentrations of hormones, IGFBP, glucose or hydroxyproline. Interaction between chromium and diabetes tended (P < 0.10) to affect maternal IGF-II concentrations, but had no effect on other maternal or fetal variables. In conclusion, maternal chromium depletion did not exacerbate hyperglycemia or pregnancy outcome in STZ-induced diabetic rats, but may negatively affect fetal protein content by decreasing fetal IGF-II concentrations. Diabetes may negatively affect fetal growth through its effect on maternal glucose, insulin and IGF-I.

L3 ANSWER 27 OF 49 MEDLINE on STN DUPLICATE 16
ACCESSION NUMBER: 1998197342 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9536279
TITLE: Immunohistochemical pattern of insulin-like growth factor (IGF) I, IGF II and IGF binding proteins 1 to 6 in carcinoma in situ of the testis.
AUTHOR: Drescher B; Lauke H; Hartmann M; Davidoff M S; Zumkeller W
CORPORATE SOURCE: Department of Anatomy, University Hospital Eppendorf, Germany.
SOURCE: Molecular pathology : MP, (1997 Dec) Vol. 50, No. 6, pp. 298-303.
Journal code: 9706282. ISSN: 1366-8714.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199804
ENTRY DATE: Entered STN: 7 May 1998
Last Updated on STN: 7 May 1998
Entered Medline: 24 Apr 1998

AB AIM: To study the immunohistochemical localisation of insulin-like growth factor (IGF) I, IGF II, and IGF binding proteins 1-6 in intratubular germ cell neoplasia in the vicinity of solid germ cell tumours of the testis. METHODS: Testes were obtained from 13 patients (20-35 years old) who had undergone orchidectomy for treatment of a solid germ cell tumour. Tumour cells were verified histologically by their distinctive morphology and by visualisation of placental alkaline phosphatase immunoreactivity. RESULTS: The majority of carcinoma in situ (CIS) cells were immunopositive for IGF I, whereas no CIS cells stained for IGF II. Of all the IGF binding proteins investigated, CIS cells showed intense immunoreactivity for IGF binding protein 5 and lower expression of all other IGF binding proteins. CONCLUSIONS: These results suggest that the action of IGF binding protein 5 in CIS cells may modulate the activity of IGF I. This may be related to a proliferative advantage that could facilitate tumour development.

L3 ANSWER 28 OF 49 MEDLINE on STN
ACCESSION NUMBER: 96366782 MEDLINE
DOCUMENT NUMBER: PubMed ID: 8770896
TITLE: The expression and characterization of human recombinant proinsulin-like growth factor II and a mutant that is defective in the O-glycosylation of its E domain.

AUTHOR: Yang C Q; Zhan X; Hu X; Kondepudi A; Perdue J F
CORPORATE SOURCE: Department of Molecular Biology, Holland Laboratory, American Red Cross, Rockville, Maryland 20855, USA.
SOURCE: Endocrinology, (1996 Jul) Vol. 137, No. 7, pp. 2766-73.
Journal code: 0375040. ISSN: 0013-7227.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199610
ENTRY DATE: Entered STN: 22 Oct 1996
Last Updated on STN: 3 Mar 2000
Entered Medline: 10 Oct 1996

AB In humans, newly synthesized proinsulin-like growth factor II (pro-IGF-II), i.e. IGF-II with an E domain extension of 89 amino acids, is 0-glycosylated on Thr75. As an approach to define the role that glycosylation of the E domain serves in the processing, secretion, and biological activities of IGF-II and to identify the sites of endoproteolytic processing, we constructed a mutant that encodes carbohydrate-free prepro-IGF-II. The mutant and wild-type prepro-IGF-II were expressed in NIH-3T3 cells, and the protein products were analyzed by SDS-PAGE followed by immunoblots with antipeptide antibodies to human and homologous rat E domain sequences. Transfectants that express glycosylated pro-IGF-II, i.e. xz97 and G11 cells, have intracellular forms of the growth factor with apparent Mr (appMr) of 21, 23, and 27K. NIH-3T3 xz95 cells, i.e. transfected with DNA that is missing the 0-glycosylation sequence, could also synthesize pro-IGF-II with an appMr of 21K. However, they did not accumulate the 23K and 27K forms of presumably glycosylated growth factor. None of the transfected NIH 3T3 cells processed much pro-IGF-II intracellularly, as the appMr 21K, 23K, and 27K forms had terminal E domain amino acid sequences that were recognized by antibodies to the homologous rat peptide sequence Met117 to Gln156. Subsequent to their secretion, the IGF-II in xz97 and G11 cells accumulated in the conditioned medium mostly as two partially processed species with appMr, of 17K and 14K, respectively. The IGF-II that accumulated in the conditioned medium of the xz95 cells had an appMr of 11K. As evidenced by a decrease in mass after treatment with neuraminidase and 0-glycosidase, the 17-kDa form of pro-IGF-II secreted by the NIH-3T3 xz97 cells was 0-glycosylated, whereas that secreted by the xz95 cells was oligosaccharide free. All of the pro-IGF-II forms have E domain amino acid sequences that reacted with antipeptide Ab to the Asp69 to Lys88 sequence. However, appMr 17K IGF-II, but not 14K IGF-II, also contained a larger E domain that was recognized by Ab to the sequence Phe89 to Arg101. The final step in the processing of 11- to 17-kDa IGF-II at Arg68 and the generation of mature IGF-II did not occur in the NIH-3T3 transfectants and is similar to what has been observed in human embryonic cells and mesenchymal tumors. The failure to remove the glycosylated E domain peptide from appMr, 14K and 17K IGF-II did not affect their binding to IGF-II /cation-independent mannose-6 phosphate receptors or presumably to IGF-I receptors, because in in vitro mitogenic assays they were equipotent with mature IGF-II. Unglycosylated pro-IGF-II from the NIH-3T3 xz95 cells also bound to these receptors. However, it was about 10 times more potent than IGF-II in stimulating thymidine incorporation into NIH-3T3 i24 IGF-IR cells, possibly because of the absence of negatively charged sialic acid and/or steric occlusion.

L3 ANSWER 29 OF 49 MEDLINE on STN DUPLICATE 17
ACCESSION NUMBER: 97036650 MEDLINE

DOCUMENT NUMBER: PubMed ID: 8882298
TITLE: Role of receptors for epidermal growth factor and insulin-like growth factors I and II in the differentiation of rat mammary glands from lactogenesis I to lactogenesis II.
AUTHOR: Bussmann L E; Bussmann I M; Charreau E H
CORPORATE SOURCE: Instituto de Biologia y Medicina Experimental-CONICET, Buenos Aires, Argentina.
SOURCE: Journal of reproduction and fertility, (1996 Jul) Vol. 107, No. 2, pp. 307-14.
Journal code: 0376367. ISSN: 0022-4251.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199612
ENTRY DATE: Entered STN: 28 Jan 1997
Last Updated on STN: 3 Mar 2000
Entered Medline: 16 Dec 1996

AB In addition to ovarian steroids and lactogenic hormones from the placenta and pituitary, growth factors control the growth and differentiation of mammary glands. Lactogenesis II at the end of pregnancy is under the control of progesterone. Ovariectomy results in a significant decrease in the number of receptors for epidermal growth factor (EGF) and insulin-like growth factor I (IGF-I) and an increase in IGF-II binding sites in mammary gland acini of rats, without affecting the affinity for their respective ligand. Although concentrations of EGF, IGF-I and IGF-II receptors are regulated by oestradiol and progesterone, replacement treatment with ovarian steroids after ovariectomy showed that receptor concentrations do not mediate the restraint on lactogenesis. Progesterone treatment, which inhibits the onset of lactogenesis II, did not restore EGF receptor concentrations to control values, and the presence of oestradiol was required to reverse the effect of ovariectomy. Oestradiol, which potentiates the effect of ovariectomy on milk synthesis, increases IGF-I receptor concentrations. IGF-II receptor concentrations, after the different steroid treatments, were consistent with the steroid effect on milk synthesis. The changes observed in the concentrations of these growth factor receptors at the onset of mammary gland secretion are not considered to affect the progesterone block to lactogenesis II, but rather are a consequence of the shift of the hormonal and, hence, physiological status of the gland.

L3 ANSWER 30 OF 49 EMBASE DUPLICATE 18
ACCESSION NUMBER: 96040834 EMBASE
DOCUMENT NUMBER: 1996040834
TITLE: The ontogeny of growth hormone, insulin-like growth factors and sex steroids: Molecular aspects.
AUTHOR: Han V.K.M.
CORPORATE SOURCE: Lawson Research Insitute, 268 Grosvenor Street,London, Ont. N6A 4V2, Canada
SOURCE: Hormone Research, (1996) Vol. 45, No. 1-2, pp. 61-66.
ISSN: 0301-0163 CODEN: HRMRA3
COUNTRY: Switzerland
DOCUMENT TYPE: Journal; Conference Article
FILE SEGMENT: 003 Endocrinology
021 Developmental Biology and Teratology
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 20 Feb 1996
Last Updated on STN: 20 Feb 1996

AB Insulin-like growth factors (IGF-1 and IGF-2) are synthesized by many tissues in response to GH treatment and

regulate cellular growth and differentiation. Fetal serum contains abundant GH, and many fetal tissues express GH receptors, but the clinical significance of GH in fetal development in humans is uncertain because hypopituitary newborns have normal birth size. The biological actions of IGFs are modulated by a family of binding proteins (IGFBPs). The demonstration of IGF and IGFBP transcripts in preimplantation embryos indicates that the influence of IGFs and IGFBPs in fetal development begins even prior to implantation. IGF and IGFBP mRNAs, except IGFBP-1 mRNA, are expressed at variable levels in many fetal tissues throughout gestation. Although the IGF mRNAs are widely expressed, IGFBP mRNAs manifest in specific cell types in a spatially and temporally specific manner, suggesting that they indicate sites of IGF action. Conditions of undernutrition and chronic hypoxemia, known to cause intrauterine growth retardation in fetuses, alter IGFBP and IGF-1 but not IGF-2 gene expression, thus indicating the role for IGF-1 and IGFBPs as mediators of altered growth. IGF and IGFBP genes are also expressed in many fetal endocrine tissues including those secreting sex steroids. Null mutation of the IGF-1 gene leads to retarded development of the primary sex organs. In the fetal adrenal gland, IGF-2 mRNA is localized to 3β-hydroxysteroid hydrogenase (3β-HSD) immunoreactive cells, suggesting a close relationship to steroid hormone biosynthesis. IGFBPs are important paracrine modulators of IGF action during development, and are crucial regulators of cellular growth and differentiation by modulating IGF-dependent or -independent actions in all tissues including developing endocrine glands.

L3 ANSWER 31 OF 49 MEDLINE on STN DUPLICATE 19
ACCESSION NUMBER: 96204041 MEDLINE
DOCUMENT NUMBER: PubMed ID: 8617668
TITLE: Effects of recombinant porcine somatotropin on placental size, fetal growth, and IGF-I and IGF-II concentrations in pigs.
AUTHOR: Sterle J A; Cantley T C; Lamberson W R; Lucy M C; Gerrard D E; Matteri R L; Day B N
CORPORATE SOURCE: Department of Animal Sciences, USDA, ARS, University of Missouri, Columbia 65211, USA.
SOURCE: Journal of animal science, (1995 Oct) Vol. 73, No. 10, pp. 2980-5.
Journal code: 8003002. ISSN: 0021-8812.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199606
ENTRY DATE: Entered STN: 20 Jun 1996
Last Updated on STN: 20 Jun 1996
Entered Medline: 13 Jun 1996

AB The objective of this study was to determine the effects of recombinant porcine somatotropin (rpST) on placental size, fetal growth, and maternal and fetal IGF-I and IGF-II concentrations. Twenty-four pregnant gilts received daily injections of either 1 mL of saline (control) (n = 12) or 5 mg of rpST (n = 12) from d 30 to 43 of gestation. Gilts were slaughtered on d 44 of gestation, reproductive tracts were removed, and fetal weight and length, placental weight, and implantation length were recorded. There was no effect of rpST on fetal or implantation length. Placental weight increased with rpST administration (71.20 +/- 3.52 vs 58.35 +/- 3.41 g; P < .02), as did fetal weight (18.06 +/- .55 vs 16.44 +/- .53 g; rpST vs control, respectively; P < .05). Implantation lengths were partitioned into quartiles to determine the effect of rpST on fetuses with different implantation lengths. The effect of rpST of fetal weight was greater in the first quartile (< 137.5 mm) than in the fourth quartile (> 240 mm) (16.04 vs 13.86 g compared with 19.47 vs 18.21 g, respectively). Analysis using a modified Brody curve suggests that the effect of rpST

treatment on fetal weight is equivalent to the effect of increasing implantation length by 58.8 mm. Administration of rpST numerically raised IGF-I (P = .07) and IGF-II (P = .12) concentrations in fetal serum. Although maternal serum IGF-I concentrations were similar at d 30, treatment with rpST increased these concentrations over time (77.76, 247.75, 267.85 vs 82.59, 79.59, 77.97 ng/mL on d 30, 37, 43, respectively; P < .001, SE = 14.09). Maternal IGF-II concentrations were also similar at d 30 but decreased over time with rpST treatment (265.78, 219.61, 191.05 vs 285.44, 284.72, 283.05 ng/mL; P < .03, SE = 14.03). Increased maternal IGF-I concentrations may exhibit negative feedback on maternal IGF-II concentrations. The more pronounced effect of rpST on growth in fetuses with shorter implantation lengths suggests that rpST may increase uptake or utilization of nutrients by fetuses. In addition, nutrient transfer across placental membranes may be enhanced by rpST.

L3 ANSWER 32 OF 49 MEDLINE on STN DUPLICATE 20

ACCESSION NUMBER: 96026599 MEDLINE
DOCUMENT NUMBER: PubMed ID: 7485832
TITLE: Effect of ethanol on plasma and hepatic insulin-like growth factor regulation in pregnant rats.
AUTHOR: Breese C R; Sonntag W E
CORPORATE SOURCE: Department of Physiology and Pharmacology, Bowman Gray School of Medicine, Wake Forest University, Winston-Salem, North Carolina, USA.
CONTRACT NUMBER: AA05315 (NIAAA)
AA08536 (NIAAA)
AG07752 (NIA)
SOURCE: Alcoholism, clinical and experimental research, (1995 Aug) Vol. 19, No. 4, pp. 867-73.
Journal code: 7707242. ISSN: 0145-6008.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199512
ENTRY DATE: Entered STN: 24 Jan 1996
Last Updated on STN: 24 Jan 1996
Entered Medline: 18 Dec 1995

AB Alcohol consumption during pregnancy has been shown to have profound developmental and behavioral effects on the fetus; however, the specific cause of these abnormalities remains unknown. These studies examined the consequences of chronic ethanol exposure during pregnancy on the regulation of maternal plasma and hepatic insulin-like growth factors (IGFs), and their associated plasma binding proteins (IGF-BPs). Ad libitum, pair, and ethanol-fed rats were fed a commercial liquid diet containing either ethanol or isocaloric maltose-dextrin from day 2 of pregnancy through parturition and killed 6 hr postpartum. Maternal plasma IGF-1 concentrations were reduced 51% in ethanol, compared with pair-fed mothers, with a corresponding 20% reduction in hepatic IGF-1 mRNA levels. In contrast, plasma IGF-2 concentrations were increased approximately 100% in ethanol-fed mothers. Whereas the smaller forms of the IGF-binding protein subunits (24 kDa and 32-29 kDa) were not affected by ethanol treatment, a significant reduction was observed in the binding subunit of IGF-BP3 (45-40 kDa) in ethanol-exposed mothers. These results suggest that alterations in plasma and hepatic IGF regulation may contribute to changes in maternal and placental metabolism and hormone regulation during pregnancy, which may in turn contribute to the intrauterine and postnatal growth retardation observed in prenatally ethanol-exposed offspring.

L3 ANSWER 33 OF 49 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN

ACCESSION NUMBER: 1995:507305 BIOSIS
DOCUMENT NUMBER: PREV199598512355
TITLE: Amniotic fluid and plasma levels of parathyroid hormone-related protein and hormonal modulation of its secretion by amniotic fluid cells.
AUTHOR(S): Dvir, Rina; Golander, Avraham; Jaccard, Niva; Yedwab, Gideon; Otremski, Itzhak; Spirer, Zvi; Weisman, Yosef [Reprint author]
CORPORATE SOURCE: Bone Dis. Unit, Tel Aviv Med. Cent., 6 Weizman St., Tel Aviv 64239, Israel
SOURCE: European Journal of Endocrinology, (1995) Vol. 133, No. 3, pp. 277-282.
ISSN: 0804-4643.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 29 Nov 1995
Last Updated on STN: 29 Nov 1995

AB Parathyroid hormone-related (PTHrP), the major mediator of humoral hypercalcemia of malignancy, may also regulate placental calcium flux, uterine contraction and fetal tissue development. In the present study, we demonstrated that the mean immunoreactive PTHrP concentrations in amniotic fluid at mid-gestation (21.2 +- 3.7 pmol/l) and at term (19.0 +- 2.7 pmol/l) were 13-16-fold higher than levels measured in either fetal (1.6 +- 0.1 pmol/l) or maternal plasma (1.4 +- 0.3 pmol/l) at term and equal to levels found in plasma of patients with humoral hypercalcemia of malignancy. In vitro studies pointed to three possible sources of PTHrP in amniotic fluid: cultured amniotic fluid cells, cells derived from the amniotic membrane overlying the placenta and placental villous core mesenchymal cells. Treatment of cultured amniotic fluid cells with human prolactin, human placental lactogen (hPL) or human growth hormone (100 mu-g/l) increased PTHrP secretion after 24 h by 43%, 109% and 90%, respectively. Insulin-like growth factors I and II (100 mu-g/l), insulin (1 00 mu-g/l) and epidermal growth factor (EGF) (10 mu-g/l) increased PTHrP secretion by 5 3%, 46%, 68% and 11 8%, respectively. The stimulation of PTHrP secretion by EGF or by hPL was both time- and dose-dependent. In contrast, calcitriol and dexamethasone (10 nmol/l) decreased PTHrP secretion by 32% and 75%, respectively. Estradiol, progesterone, dihydrotestosterone and human chorionic gonadotropin had no effect on PTHrP secretion. These findings support the notion that PTHrP may play a physiological role in the uteroplacental unit and demonstrate that human amniotic fluid cells could be a useful model for studying the regulation of PTHrP production and secretion by hormones and growth factors.

L3 ANSWER 34 OF 49 MEDLINE on STN DUPLICATE 21
ACCESSION NUMBER: 95197949 MEDLINE
DOCUMENT NUMBER: PubMed ID: 7534329
TITLE: A homologous radioimmunoassay for ovine insulin-like growth factor-binding protein-2: ontogenesis and the response to growth hormone, placental lactogen and insulin-like growth factor-I treatment in sheep.
AUTHOR: Gallaher B W; Breier B H; Blum W F; McCutcheon S N; Gluckman P D
CORPORATE SOURCE: Department of Paediatrics, University of Auckland, New Zealand.
SOURCE: The Journal of endocrinology, (1995 Jan) Vol. 144, No. 1, pp. 75-82.
Journal code: 0375363. ISSN: 0022-0795.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199504
ENTRY DATE: Entered STN: 27 Apr 1995

Last Updated on STN: 29 Jan 1996
Entered Medline: 18 Apr 1995

AB Although insulin-like growth factor-binding protein-2 (IGFBP-2) is an abundant IGFBP in fetal and postnatal plasma, its regulation is not yet clearly understood. To address this question in sheep, we purified ovine IGFBP-2 and developed a homologous radioimmunoassay. We have studied its ontogenesis and measured serum concentrations of ovine IGFBP-2 after bovine growth hormone (bGH), ovine placental lactogen (oPL) and IGF-I treatment. Concentrations of IGFBP-2 were high at 125 days of gestation (550 +/- 15 micrograms/l) but fell after birth ($P < 0.05$) and plateaued after 1 year of age (340 +/- 20 micrograms/l). In lactating ewes, bGH treatment for 7 days significantly reduced (21%; $P < 0.05$) IGFBP-2 relative to the saline-treated group. Similarly, in neonatal lambs, bGH treatment from day 3 to day 23 of life reduced ($P < 0.05$) IGFBP-2 by 23% relative to the saline-treated group. oPL had no effect on serum levels of IGFBP-2 in the ewe or the neonatal lamb. In well-fed yearling lambs, treatment with IGF-I reduced IGFBP-2 values by 27% ($P < 0.05$) relative to control animals. In yearling lambs, reduced nutrition increased plasma IGFBP-2 (41%; $P < 0.05$). However this increase was abolished by IGF-I treatment. The changes in plasma levels of IGFBP-2 were positively related to changes in IGF-II while there was a negative relationship between circulating IGF-I and IGFBP-2 such that both IGF-I and IGF-II may play a role in the regulation of IGFBP-2 in serum.

L3 ANSWER 35 OF 49 MEDLINE on STN DUPLICATE 22
ACCESSION NUMBER: 94257753 MEDLINE
DOCUMENT NUMBER: PubMed ID: 8199260
TITLE: Characterization, localization, and regulation of receptors for insulin-like growth factor I in the baboon uterus during the cycle and pregnancy.
AUTHOR: Hild-Petito S; Verhage H G; Fazleabas A T
CORPORATE SOURCE: Department of Obstetrics and Gynecology, University of Illinois, Chicago 60612-7313.
CONTRACT NUMBER: HD-07508339 (NICHD)
HD-21991 (NICHD)
SOURCE: Biology of reproduction, (1994 Apr) Vol. 50, No. 4, pp. 791-801.
Journal code: 0207224. ISSN: 0006-3363.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199407
ENTRY DATE: Entered STN: 14 Jul 1994
Last Updated on STN: 3 Mar 2000
Entered Medline: 5 Jul 1994

AB The objective of this study was to determine the presence, regulation, and localization of specific receptors for insulin-like growth factor I (IGF-I) in primate reproductive tissues. Uteri were obtained from baboons either during the menstrual cycle, after ovariectomy with or without steroid treatments, or during early pregnancy (Days 18-60 postovulation [PO]). Placental and decidual tissues were collected from baboons during late pregnancy (Days 130-160). Localization of type I IGF receptor was determined by indirect immunocytochemistry (alpha IR3 antibody), and levels of type I IGF receptors were determined by affinity cross-linking and binding assays. Specific staining for type I IGF receptors was present in the membranes of glandular epithelial cells throughout the cycle and early pregnancy; however, there was a decrease in staining intensity by the late luteal phase and also throughout early pregnancy compared to the late follicular phase. Specific receptor staining was absent in stromal cells throughout the cycle. By Day 19 PO, stromal cells directly under the trophoblast were positive for type I IGF receptor, and an increase in stromal staining at the implantation site was

observed as pregnancy proceeded. Stromal staining was apparent in non-implantation site tissue by Day 32 PO. Some placental villi showed positive receptor staining as early as on Day 18 PO, and an increase in the number of positive villi was apparent as pregnancy progressed. An 125I-IGF-I-protein complex of approximately 140,000 daltons, corresponding to the alpha subunit of the type I IGF receptor, was detected in endometrial, placental, and decidual membranes. The intensity of this signal was high in endometrium from the follicular phase, whereas low levels were detected in endometrium from the luteal phase. Throughout early pregnancy, alpha receptor subunit was present in placental and decidual membranes; alpha receptor subunit increased in placenta as pregnancy proceeded. An additional 125I-IGF-I-protein complex of 43,000 daltons, corresponding to IGF binding protein-1 (IGFBP-1), was present in decidual membranes and appeared to increase as pregnancy proceeded. Specific binding of 125I-IGF-I to placental membranes was displaced by unlabeled IGF-I and alpha IR3 antibody, whereas both unlabeled IGF-I and IGF-II competed equally for binding to decidual membranes. Scatchard analysis of 125I-IGF-I binding to placental membranes revealed a single class of high-affinity receptors (KD = 2.35 +/- 0.8 nM; mean +/- SEM).(ABSTRACT TRUNCATED AT 400 WORDS)

L3 ANSWER 36 OF 49 MEDLINE on STN DUPLICATE 23
ACCESSION NUMBER: 95045587 MEDLINE
DOCUMENT NUMBER: PubMed ID: 7957246
TITLE: Insulin-like growth factor-II is a substrate for dipeptidylpeptidase I (cathepsin C). Biological properties of the product.
AUTHOR: Kiess W; Terry C; Burgess W H; Linder B; Lopaczynski W; Nissley P
CORPORATE SOURCE: Metabolism Branch, National Cancer Institute, National Institute of Child Health and Human Development, National Institutes of Health, Bethesda.
SOURCE: European journal of biochemistry / FEBS, (1994 Nov 15) Vol. 226, No. 1, pp. 179-84.
Journal code: 0107600. ISSN: 0014-2956.
PUB. COUNTRY: GERMANY: Germany, Federal Republic of
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199412
ENTRY DATE: Entered STN: 10 Jan 1995
Last Updated on STN: 3 Mar 2000
Entered Medline: 28 Dec 1994

AB We observed that the lysosomal enzyme, dipeptidylaminopeptidase I (DAP-I) caused the release of trichloroacetic-acid-soluble radioactivity from rat 125I-insulin-like growth factor-II (IGF-II). This activity could be blocked by dipeptide inhibitors of DAP-I, and was enhanced by chloride. Treatment of unlabeled rat IGF-II with DAP-I converted approximately 50% of the IGF-II to a species with a slightly shorter elution time on reverse-phase HPLC, whereas treatment of human IGF-II caused complete conversion to the species with the shorter elution time. Rat IGF-II purified from the rat BRL 3A cell line is a mixture of two molecules beginning with Ala-Tyr-Arg-Pro-Ser- and Tyr-Arg-Pro-Ser- [Marquardt, H., Todaro, G. J., Henderson, L. E. & Oroszlan, S. (1981) J. Biol. Chemical 256, 6859-6865] while human IGF-II begins with Ala-Tyr-Arg-Pro-Ser-. Determination of the N-terminal amino acid sequence of human IGF-II before and after digestion with DAP-I showed that DAP-I cleaved Ala-Tyr, terminating at Arg-Pro-; the rat IGF-II species beginning with Tyr-Arg-Pro-Ser- was resistant to digestion. In order to compare DAP-I-treated IGF-II with native IGF-II for binding to IGF receptors and IGF-binding

proteins and in a bioassay, rat and human IGF-II were treated with DAP-I and the digested and undigested species were isolated by reverse-phase HPLC. The IGF-II/mannose 6-phosphate receptor was purified from rat placental membranes, the IGF-I receptor was solubilized from human placental membranes and IGF-binding proteins were partially purified from adult and three-day-old rat sera by sequential gel filtration on Sephadex G-200 (pH 8.0) and Sephadex G-50 (acid pH). The dose/response curves of the two IGF -II species were indistinguishable in radioreceptor assays utilizing the IGF-II/mannose 6-phosphate receptor and the IGF-I receptor and in IGF competitive binding assays utilizing partially purified IGF-binding proteins. The DAP-I-digested and native IGF-II species were also equipotent in stimulating [3H]thymidine incorporation into DNA in the human osteosarcoma cell line, MG-63. We conclude that DAP-I cleaves an N-terminal dipeptide from IGF-II and that this does not result in a change in the biological activity of the molecule.

L3 ANSWER 37 OF 49 EMBASE COPYRIGHT (c) 2007 Elsevier B.V. All rights reserved on STN DUPLICATE 24

ACCESSION NUMBER: 94138976 EMBASE
DOCUMENT NUMBER: 1994138976
TITLE: Effect of ethanol on insulin-like growth factor-II release from fetal organs.
AUTHOR: Mauceri H.J.; Lee W.-H.; Conway S.
CORPORATE SOURCE: Department of Biological Sciences, Northern Illinois University,DeKalb, IL 60115-2861, United States
SOURCE: Alcoholism: Clinical and Experimental Research, (1994) Vol. 18, No. 1, pp. 35-41.
ISSN: 0145-6008 CODEN: ACRSDM
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 003 Endocrinology
010 Obstetrics and Gynecology
021 Developmental Biology and Teratology
040 Drug Dependence, Alcohol Abuse and Alcoholism
052 Toxicology
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 2 Jun 1994
Last Updated on STN: 2 Jun 1994

AB This study examines the effect of ethanol (ETOH) exposure and nutrient restriction on the release of insulin-like growth factor (IGF)-II from 18- and 20-day explanted fetal organs. Fetuses were exposed to ETOH (E) in utero by feeding dams a 36% (calories derived from ETOH: 6.6% v/v) ETOH liquid diet. Control fetuses were offsprings of dams either pair-fed (P) a control liquid diet or ad libitum (A) fed a standard pelleted lab chow. Brain, heart, kidney, liver, lung, muscle, and placenta of fetuses from the same litter were pooled and explanted, and IGF-II concentration in explanted media was analyzed by radioimmunoassay. Maternal and fetal weights were determined during pregnancy and at sacrifice, respectively, to evaluate the influence of ETOH on growth. Both maternal and fetal weights were substantially reduced by ETOH on 18 and 20 days of gestation compared with both A and P controls. At 18 days of gestation, E fetuses (1.33 ± 0.03 g) weighed less than either A (1.47 ± 0.03 g) or P (1.54 ± 0.04 g) fetuses. By 20 days, A mean fetal weight (4.19 ± 0.23 g) was significantly greater than both P (3.74 ± 0.06 g) and E (3.28 ± 0.06 g) fetuses. IGF-II concentration in media from 18-day fetal explants was highest from E (brain, heart, liver, and placenta) and P tissues (kidney, lung, and muscle). IGF-II in media from A tissues (except placenta) was lower than both E and P levels. A significant difference between treatments occurred in heart. By 20 days, IGF-

II levels were highest in media from all A tissues (except placenta). IGF-II in media from E tissues (except lung) was lower than those from P tissues. A significant difference between treatments occurred in the brain. With regard to the developmental pattern, IGF-II release generally increased between 18 and 20 days of gestation, with the greatest increases occurring in A tissues. Increased secretion by P tissues was greater than that by corresponding E tissues, and tended to follow the A trend. On the other hand, E brain, kidney, and placenta released only slightly more IGF-II at 20 days compared to 18 days, whereas E heart, liver, lung, and muscle released slightly less hormone. This study suggests that even moderate nutrient deprivation influences the pattern of IGF-II release from fetal organs, even though there is only a small decrease in overall body size. At the same level of nutrient deprivation, ETOH more dramatically alters both fetal weight and the pattern of IGF-II release. Because IGFs are autocrine/paracrine factors that influence growth, differentiation, and function, the reduced availability of IGF-II may be one of the factors contributing to ETOH-induced growth retardation and impaired functional capacity of some organ systems.

L3 ANSWER 38 OF 49 MEDLINE on STN DUPLICATE 25

ACCESSION NUMBER: 94106246 MEDLINE
DOCUMENT NUMBER: PubMed ID: 7506472
TITLE: IGFBP-2 expression in liver and mammary tissue in lactating and pregnant ewes.
AUTHOR: Klempt M; Breier B H; Min S H; MacKenzie D D; McCutcheon S N; Gluckman P D
CORPORATE SOURCE: Research Centre for Developmental Medicine and Biology, School of Medicine, University of Auckland, New Zealand.
SOURCE: Acta endocrinologica, (1993 Nov) Vol. 129, No. 5, pp. 453-7.
Journal code: 0370312. ISSN: 0001-5598.
PUB. COUNTRY: Denmark
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199402
ENTRY DATE: Entered STN: 18 Feb 1994
Last Updated on STN: 29 Jan 1996
Entered Medline: 4 Feb 1994

AB Binding proteins for the insulin-like growth factors (IGFBPs) modulate the actions of IGF I and IGF II. IGFBP-2 is particularly high in plasma of pregnant and fetal animals and in milk. We investigated the peri-lactational control of IGFBP-2 expression and secretion. Fifteen singleton-bearing pregnant ewes at day 101 of gestation were injected sc twice daily for 8 days with bovine growth hormone (bGH) or ovine placental lactogen (oPL) both at 0.15 mg.kg-1.d-1 or saline. A further fifteen ewes at day 17 of lactation were injected sc twice daily for 5 days with bGH or oPL at 0.1 mg.kg-1.d-1 or saline. On the last day of injection blood samples were taken and the animals were sacrificed. Liver and mammary tissue samples were immediately frozen and subsequently extracted to provide total RNA for evaluation by Northern blot analysis using a rat IGFBP-2 cDNA probe. Plasma samples were analysed by Western ligand blotting for IGFBP-2. The comparison of the two saline-treated groups (pregnant vs lactating ewe) revealed no difference in the plasma concentrations of IGFBP-2. IGFBP-2 mRNA expression in the liver of the lactating ewes was markedly increased compared to that in the pregnant ewes. In contrast, in mammary tissue the expression was significantly lower in lactating than in pregnant sheep. In pregnant animals treatment with bGH, but not oPL, decreased the expression of IGFBP-2 in liver. There was a similar trend in the lactating ewe.(ABSTRACT TRUNCATED AT 250 WORDS)

L3 ANSWER 39 OF 49 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1994:97139 CAPLUS
DOCUMENT NUMBER: 120:97139
TITLE: Physiological and pathological changes of insulin-like growth factor-II and its binding proteins in infancy and childhood
AUTHOR(S): Takeya, Ryohei
CORPORATE SOURCE: Sch. of Med., Kanazawa Univ., Kanazawa, 920, Japan
SOURCE: Kanazawa Daigaku Juzen Igakkai Zasshi (1993), 102(2), 214-27
CODEN: JUZIAG; ISSN: 0022-7226
DOCUMENT TYPE: Journal
LANGUAGE: Japanese
AB By using a newly-developed insulin-like growth factor II (IGF-II) RIA, I examined clin. IGF-II levels and its specific binding proteins (IGFBP), and also studied IGF-II systems in rat models of intrauterine growth retardation (IUGR) by maternal fasting or dexamethasone treatment. Cord blood IGF-II levels, were significantly correlated with gestational weeks and birth wts. During childhood, there were no apparent changes in serum IGF-II values. Serum IGF-II levels were elevated in late pregnancy and returned to the normal level within a few days after delivery, indicating the relation between maternal IGF-II and feto-placental unit. Cord blood IGF-II levels of small for date (SFD) infants were significantly lower than those of age-matched appropriate for date (AFD) infants, suggesting the involvement of IGF-II in IUGR. In SFD infants, Western ligand anal. showed an increment of serum IGFBP-1 and a reduction of BP-3 in comparison with those in AFD infants. In IUGR rats, tissue IGF-II contents were decreased and a similar serum IGFBP pattern to SFD infants was observed The binding capacity of tissue IGF-II receptor was higher than those of control rats. These results suggested that IGF-II systems play a crucial role in fetal growth. In patients with growth hormone (GH) deficiency, hepatic dysfunction, ulcerative colitis and insulin-dependent diabetes mellitus, serum IGF-II levels were decreased in the active stage of the diseases and normalized in the convalescent stage. These results suggested that serum IGF-II levels were influenced by several factors, such as GH, hepatic reserve, nutritional state and glycemic control. In chronic renal failure, there was a significant increment of serum IGF-II levels, and the higher mol. forms of IGF-II (12 and 15kD) were definitely detected on Western anal., which was probably due to an impairment of renal clearance. Urinary IGF-II levels were not influenced by age, and in nephrotic syndrome, urinary IGF-II values were not significantly different from those of control subjects and also not affected by the degree of urinary occult blood or protein contents. On Western ligand anal. of urinary IGFBP, BP-2 and BP-3 were increased in the cases of glomerulopathy, whereas BP-1 was increased in renal tubular dysfunction. Although urinary IGF-II alone can not be a clin. indicator in nephrotic disease, urinary IGFBP patterns may be a useful marker in the diagnosis of renal impairment. CSF IGF-II levels were also not influenced by age and increased in some cases of encephalitis. CSF IGFBP mainly consisted of IGFBP-1 and BP-2; BP-2 showed a higher affinity for IGF-II than IGF-I, and increased generally in a number of CNS diseases. These IGFBP dynamics may be important in understanding the local bioavailability of IGF-II in CNS.

L3 ANSWER 40 OF 49 MEDLINE on STN DUPLICATE 26
ACCESSION NUMBER: 94063325 MEDLINE
DOCUMENT NUMBER: PubMed ID: 8243887
TITLE: Wilms' tumor (WT1) gene expression in rat decidual

differentiation.
AUTHOR: Zhou J; Rauscher F J 3rd; Bondy C
CORPORATE SOURCE: Developmental Endocrinology Branch NICHD, NIH, Bethesda, MD 20892.
CONTRACT NUMBER: CA 10817 (NCI)
CA 47983 (NCI)
CA 52009 (NCI)
SOURCE: Differentiation; research in biological diversity, (1993 Sep) Vol. 54, No. 2, pp. 109-14.
Journal code: 0401650. ISSN: 0301-4681.
PUB. COUNTRY: GERMANY: Germany, Federal Republic of
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199312
ENTRY DATE: Entered STN: 1 Feb 1994
Last Updated on STN: 3 Mar 2000
Entered Medline: 23 Dec 1993

AB The Wilm's tumor suppressor gene (WT1) encodes a zinc-finger containing transcription factor that is selectively expressed in the developing urogenital tract, where it is thought to play a role in the differentiation of these tissues. We have used immunocytochemistry and in situ hybridization to study WT1 expression in the rat uterus during normal development and pregnancy from 0 to 20 days post coitum (p.c.). WT1 mRNA was abundant in uterine stroma from juvenile rats, but was much less abundant in uterine tissue from sexually mature rats; WT1 expression is not affected by ovariectomy or by treatment with estradiol or estradiol plus progesterone. WT1 gene was highly expressed, however, in the endometrial cells of early pregnancy. On day 6 p.c. WT1 mRNA was detected in anti-mesometrial decidual cells, and WT1 immunoreactivity was concentrated in the nuclei of these cells. All cells of fully-developed deciduoma at 7-8 days p.c. demonstrated WT1 expression. WT1 was not detected in trophoblast/placental tissues but remained abundant in the decidua basalis until parturition. The expression of WT1 was compared with insulin-like growth factor-II (IGF-II) and its receptor in the decidual since it has been shown that IGF -II gene transcription is repressed by WT1 in vitro. However, no spatiotemporal correlation in the expression of these three genes was found in differentiation of the rat decidua. In summary, these data suggest a role for WT1 in decidualization, since its expression is activated during the differentiation of uterine stromal cells into decidual cells.

L3 ANSWER 41 OF 49 MEDLINE on STN DUPLICATE 27
ACCESSION NUMBER: 92164521 MEDLINE
DOCUMENT NUMBER: PubMed ID: 1537293
TITLE: Constitutive synthesis of insulin-like growth factor-II by primary osteoblast-enriched cultures from fetal rat calvariae.
AUTHOR: McCarthy T L; Centrella M; Canalis E
CORPORATE SOURCE: Department of Research, Saint Francis Hospital and Medical Center, Hartford, Connecticut 06105.
CONTRACT NUMBER: DK-42424 (NIDDK)
SOURCE: Endocrinology, (1992 Mar) Vol. 130, No. 3, pp. 1303-8.
Journal code: 0375040. ISSN: 0013-7227.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199204
ENTRY DATE: Entered STN: 17 Apr 1992
Last Updated on STN: 17 Apr 1992
Entered Medline: 2 Apr 1992

AB While a number of osteotropic hormones regulate insulin-like growth

factor-I (IGF-I) synthesis in osteoblast-enriched (Ob) and intact bone cultures, their direct effects on IGF-II production are still unresolved. For example, cAMP stimulators, such as PTH and prostaglandin E2, increase Ob IGF-I transcript and polypeptide levels within the first 24 h of treatment, but have no effect on IGF-II expression. To examine the possibility that other circulating factors could directly modify IGF-II synthesis by osteoblasts, primary rat Ob cultures were briefly treated with a number of polypeptide and steroid hormones known to regulate bone metabolism. Prepro-IGF-II steady state transcripts were assessed by Northern blot analysis, and immunoreactive polypeptide levels (iIGF-II) were examined by RIA. Predominant prepro-IGF-II transcripts of 3.7 kilobases were readily detected in quiescent Ob cultures, and constitutive iIGF-II levels were approximately 2-7 nM throughout the first 24 h of culture. GH, placental lactogen, insulin, cortisol, testosterone, T3, 17 beta-estradiol, and 1,25-dihydroxyvitamin D3 each had no effect on prepro-IGF-II transcripts within 6 h or on iIGF-II polypeptide expression within a 24-h period. These studies indicate that IGF-II synthesis is constitutive in unstimulated primary fetal rat Ob cultures, and that these levels are not directly modulated by short term treatment with a variety of osteotropic hormones.

L3 ANSWER 42 OF 49 MEDLINE on STN DUPLICATE 28

ACCESSION NUMBER: 92306862 MEDLINE
DOCUMENT NUMBER: PubMed ID: 1377124
TITLE: Expression of a lactogen-dependent insulin-like growth factor-binding protein in cultured mouse mammary epithelial cells.
AUTHOR: Fielder P J; Thordarson G; English A; Rosenfeld R G; Talamantes F
CORPORATE SOURCE: Department of Pediatrics, Stanford University Medical School, California 94305.
CONTRACT NUMBER: DK-08516-01 (NIDDK)
DK-28229 (NIDDK)
HD-14966 (NICHD)
+
SOURCE: Endocrinology, (1992 Jul) Vol. 131, No. 1, pp. 261-7.
Journal code: 0375040. ISSN: 0013-7227.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199207
ENTRY DATE: Entered STN: 7 Aug 1992
Last Updated on STN: 29 Jan 1996
Entered Medline: 27 Jul 1992

AB The ability of normal mouse mammary epithelial cells (MECs) to express insulin-like growth factor-binding proteins (IGFBPs) was examined. MECs were isolated from day 11 pregnant mice and cultured on floating collagen gels in serum-free basal medium. After 24 h, the medium was replaced with fresh medium with/or without mouse PRL (mPRL), mouse placental lactogen-I (mPL-I), mPL-II, mouse GH (mGH), IGF-I, and IGF-II, either alone or in combinations. The MECs were cultured for an additional 5 days before collection of conditioned medium (CM). The relative amount of IGFBPs present in the CM was determined by Western ligand blotting, and alpha-lactalbumin content was determined with a specific RIA. The CM of the MECs contained two IGFBPs, with approximate mol wt of 29K and 40-45K. The 40-45K IGFBP appears to be the mouse equivalent of IGFBP-3, but the identity of the 29K IGFBP is not presently known. The 29K IGFBP was not N-glycosylated and did not cross-react with antiserum to rodent IGFBP-2 or human IGFBP-1. Basal IGFBP expression was very low, but the addition of mPL-I, or mPL-II stimulated a marked increase in the amount of 29K IGFBP that was released into the CM and a

lesser increase in the release of IGFBP-3. This increase in the release of 29K IGFBP was dose dependent, with increases found at concentrations as low as 1 ng/ml lactogen. mGH also stimulated the release of 29K IGFBP, but was less potent than any of the three lactogens. Treatment of MECs with either IGF-I or IGF-II increased the amount of both the 29K IGFBP and IGFBP-3 in the CM, with relative potencies similar to those of the lactogenic hormones. However, when either IGF-I or IGF-II was added together with one of the lactogenic hormones, the release of 29K IGFBP was increased in an additive manner. While the IGFs acted additively with the lactogenic hormones on the expression of 29K IGFBP, they did not stimulate alpha-lactalbumin production by the MECs or act to enhance the effects of the lactogenic hormones in stimulating alpha-lactalbumin production. This study demonstrates that IGFBPs are expressed in normal mouse MECs, and the release of these IGFBPs into the CM is hormonally regulated by both lactogenic hormones and IGFs.

L3 ANSWER 43 OF 49 MEDLINE on STN DUPLICATE 29
ACCESSION NUMBER: 92176866 MEDLINE
DOCUMENT NUMBER: PubMed ID: 1541918
TITLE: Serum half-life and in-vivo actions of recombinant bovine placental lactogen in the dairy cow.
AUTHOR: Byatt J C; Eppard P J; Veenhuizen J J; Sorbet R H; Buonomo F C; Curran D F; Collier R J
CORPORATE SOURCE: Monsanto Company, St Louis, Missouri 63198.
SOURCE: The Journal of endocrinology, (1992 Feb) Vol. 132, No. 2, pp. 185-93.
Journal code: 0375363. ISSN: 0022-0795.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199204
ENTRY DATE: Entered STN: 24 Apr 1992
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Entered Medline: 7 Apr 1992

AB The clearance rate of recombinant bovine placental lactogen (rbPL) from the blood serum of four lactating dairy cows was measured using a specific radioimmunoassay. Two animals were non-pregnant, while the other two were at approximately 120 days of gestation. The rbPL was administered as an i.v. bolus injection (4 mg total) via an indwelling jugular catheter. Blood samples were taken periodically for 180 min and assayed for rbPL. Analysis of the clearance curves for the bolus injection suggested a single-compartment model and a serum half-life of 7.25 min. In a second experiment with the same animals, following cessation of lactation, rbPL or bovine GH (bGH) were administered by s.c. injection (50 mg/day) for 5 consecutive days. Blood samples were taken twice per day during the treatment period and a 3-day pretreatment period. Samples were analysed for glucose, blood urea nitrogen (BUN), non-esterified fatty acids (NEFA), creatinine, insulin, insulin-like growth factor-I (IGF-I) and IGF-II, tri-iodothyronine (T3), progesterone and IGF-binding protein-2 (IGFBP-2) to determine whether rbPL mediates similar metabolic effects to those of bGH. Administration of bGH stimulated an increase in NEFA, glucose, T3 and insulin, whereas none of these variables was affected by rbPL. The plasma concentrations of IGF-I and IGF-II were both increased by treatment with rbPL but, to a lesser extent than occurred with bGH. Interestingly, BUN and IGFBP-2 concentrations were reduced equally by bGH and rbPL. These results suggest that rbPL does not necessarily act as a GH agonist but, rather, may have distinct effects on intermediary metabolism that could be mediated through another specific receptor.

L3 ANSWER 44 OF 49 MEDLINE on STN DUPLICATE 30

ACCESSION NUMBER: 92063866 MEDLINE
DOCUMENT NUMBER: PubMed ID: 1954892
TITLE: Influence of the fetus and estrogen on maternal serum growth hormone, insulin-like growth factor-II, and epidermal growth factor concentrations during baboon pregnancy.
AUTHOR: Putney D J; Henson M C; Pepe G J; Albrecht E D
CORPORATE SOURCE: Department of Obstetrics/Gynecology, University of Maryland School of Medicine, Baltimore 21201.
CONTRACT NUMBER: R01-HD-13294 (NICHD)
T32-HD-07170 (NICHD)
SOURCE: Endocrinology, (1991 Dec) Vol. 129, No. 6, pp. 3109-17.
Journal code: 0375040. ISSN: 0013-7227.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199112
ENTRY DATE: Entered STN: 24 Jan 1992
Last Updated on STN: 3 Mar 2000
Entered Medline: 27 Dec 1991

AB In the present study we determined whether the fetus and estrogen affect maternal serum concentrations of GH, insulin-like growth factor-II (IGF-II), and epidermal growth factor (EGF) and placental IGF-II formation in pregnant baboons. The objective was to ascertain whether the previously reported increase in placental formation and serum concentrations of IGF-I induced by removal of the fetus and, thus, estrogen in pregnant baboons was mediated by GH and whether it was specific for IGF-I. On day 100 of gestation (term is 184 days), fetuses were removed, and placentas were left in situ, i.e. fetectomy. After fetectomy, baboons received pellets of aromatizable androstenedione (50-150 mg every 10 days, sc; n = 8), were injected with estradiol (E2) benzoate (0.50-2.5 mg/day, sc; n = 8), or were not further treated (n = 6) on days 101-159 of gestation. Placental cells obtained on day 160 were dispersed in 0.1% collagenase, isolated via 50% Percoll centrifugation, then incubated for 24 h at 37 C in medium 199. Maternal serum E2 concentrations increased with advancing gestation in intact baboons, were decreased by 79% after fetectomy and, thus, removal of adrenal C-19 steroid estrogen precursors, and restored by androstenedione or E2 treatment after fetectomy. Mean serum GH was 20.2 +/- 0.6 ng/ml on days 101-160 in untreated intact animals. Fetectomy decreased (P less than 0.001) GH levels to 12.1 +/- 0.5 ng/ml. Androstenedione or E2 treatment after fetectomy restored serum GH to 20.8 +/- 1.1 and 22.4 +/- 0.6 ng/ml, respectively. Serum IGF-II was 1406 +/- 54 ng/ml on days 101-160 in controls and decreased (P less than 0.001) rapidly after fetectomy to a value (305 +/- 16) that was 78% lower than that in untreated baboons. Androstenedione or E2 treatment after fetectomy had no effect on the fetectomy-induced decrease in IGF-II levels. In vitro secretion of IGF-II by placental trophoblasts of fetectomized baboons (10.3 +/- 0.6 ng/ml.24 h) was 88% lower (P less than 0.001) than that in controls (85.6 +/- 15.7). Despite androstenedione or E2 treatment after fetectomy, placental IGF-II production remained low (9.2 +/- 1.1 and 8.8 +/- 0.4 ng/ml.24 h, respectively). The overall mean maternal serum EGF concentration was 379 +/- 20 pg/ml in the second half of baboon pregnancy. Fetectomy or treatment with androstenedione or E2 had no effect on serum EGF levels.(ABSTRACT TRUNCATED AT 400 WORDS)

L3 ANSWER 45 OF 49 MEDLINE on STN DUPLICATE 31
ACCESSION NUMBER: 92037361 MEDLINE
DOCUMENT NUMBER: PubMed ID: 1935779
TITLE: Regulation of insulin-like growth factor-II production in

bone cultures.
AUTHOR: Canalis E; Centrella M; McCarthy T L
CORPORATE SOURCE: Department of Research, Saint Francis Hospital and Medical Center, Hartford, Connecticut 06105.
CONTRACT NUMBER: DK-42424 (NIDDK)
SOURCE: Endocrinology, (1991 Nov) Vol. 129, No. 5, pp. 2457-62.
Journal code: 0375040. ISSN: 0013-7227.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199112
ENTRY DATE: Entered STN: 24 Jan 1992
Last Updated on STN: 24 Jan 1992
Entered Medline: 2 Dec 1991

AB Although bone matrix is a rich source of insulin-like growth factor-II (IGF-II), little is known about the regulation of its synthesis by bone cells. This is due in part to the lack of simple and reliable assays to measure IGF-II. We have developed a method to dissociate IGF-II from its binding proteins by acidification and ultrafiltration, and quantitated IGF -II by RIA in 24- to 72-h cultures of 21-day-old fetal rat calvariae. The coefficient of variation of the assay was 13.8% or less; the recovery of IGF-II was 30-50%, and IGF-I cross-reacted 1% or less in the assay compared to IGF-II standards. The IGF-II concentrations in calvarial culture medium were in the 1- to 3-nM range, and these levels were suppressed by cycloheximide (3.6 microM) by almost 80%. Continuous treatment with placental lactogen, PTH, GH, insulin, or T3 did not modify IGF-II concentrations in 24- to 72-h cultures. Treatment with 17 beta-estradiol, testosterone, and 1,25-dihydroxyvitamin D3 also had no effect on IGF-II levels, whereas cortisol (10-100 nM) decreased IGF-II concentrations by 20-50%. Transforming growth factor-beta, prostaglandin E2, and platelet-derived growth factor BB did not alter IGF-II levels, and basic fibroblast growth factor (0.06-6 nM) for 72 h decreased calvarial IGF-II by 30-50%. In conclusion, 21-day-old fetal rat calvariae secrete IGF-II, and its concentration in culture medium is decreased by cortisol and basic fibroblast growth factor.

L3 ANSWER 46 OF 49 MEDLINE on STN DUPLICATE 32
ACCESSION NUMBER: 91206548 MEDLINE
DOCUMENT NUMBER: PubMed ID: 1673320
TITLE: GRF treatment of late pregnant ewes alters maternal and fetal somatotropic axis activity.
AUTHOR: Blanchard M M; Goodyer C G; Charrier J; Kann G; Garcia-Villar R; Bousquet-Melou A; Toutain P L; Barenton B
CORPORATE SOURCE: Institut National de la Recherche Agronomique, Unite de Differenciation Cellulaire et Croissance, Montpellier, France.
SOURCE: The American journal of physiology, (1991 Apr) Vol. 260, No. 4 Pt 1, pp. E575-80.
Journal code: 0370511. ISSN: 0002-9513.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199105
ENTRY DATE: Entered STN: 7 Jun 1991
Last Updated on STN: 6 Feb 1995
Entered Medline: 17 May 1991

AB To examine the effects of anabolic agents given during late gestation on the maternal and fetal somatotropic axes, we injected pregnant ewes twice

daily with 0.15 mg somatocrinin (GRF)-(1-29) for 10 days beginning on day 130 of gestation. Maternal and fetal endocrine changes were compared with control animals using both in vivo and in vitro approaches. Treatment with GRF increased maternal plasma levels of growth hormone (GH) and insulin-like growth factor I (IGF-I;P less than 0.05) but not IGF-II. Under in vitro test conditions, maternal pituitary cells showed a greater maximal response (P less than 0.001) to GRF. In the fetuses of treated ewes, cord plasma GH levels were not significantly increased compared with controls. These animals had similar IGF-I but higher IGF-II (P less than 0.05) plasma levels. The maximal response of fetal pituitary cells to GRF was increased (P less than 0.001). GRF treatment had no influence on maternal and fetal pituitary cell responses to somatostatin under either basal or GRF-stimulated conditions. In addition, these treatments did not affect plasma levels of placental lactogen, glucose, or free fatty acids in the maternal and fetal sheep. These data are compatible with the hypothesis that treatment of pregnant ewes in the last days of gestation with GRF could support accelerated fetal growth.

L3 ANSWER 47 OF 49 EMBASE

ACCESSION NUMBER: 91180674 EMBASE
DOCUMENT NUMBER: 1991180674
TITLE: GRF treatment of late pregnant ewes alters maternal and fetal somatotropic axis activity.
AUTHOR: Blanchard M.M.; Goodyer C.G.; Charrier J.; Kann G.; Garcia-Villar R.; Bousquet-Melou A.; Toutain P.L.; Barenton B.
CORPORATE SOURCE: INRA-ENSA, Unite de Differenciation, Cellulaire et Croissance, 2, Place P. Viala,34060 Montpellier-Cedex, France
SOURCE: American Journal of Physiology - Endocrinology and Metabolism, (1991) Vol. 260, No. 4 23-4, pp. E575-E580. . ISSN: 0002-9513 CODEN: AJPMD
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 003 Endocrinology
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 16 Dec 1991
Last Updated on STN: 16 Dec 1991

AB To examine the effects of anabolic agents given during late gestation on the maternal and fetal somatotropic axes, we injected pregnant ewes twice daily with 0.15 mg somatocrinin (GRF)-(1-29) for 10 days beginning on day 130 of gestation. Maternal and fetal endocrine changes were compared with control animals using both in vivo and in vitro approaches. Treatment with GRF increased maternal plasma levels of growth hormone (GH) and insulin-like growth factor I (IGF-I; $P < 0.05$) but not IGF-II. Under in vitro test conditions, maternal pituitary cells showed a greater maximal response ($P < 0.001$) to GRF. In the fetuses of treated ewes, cord plasma GH levels were not significantly increased compared with controls. These animals had similar IGF-I but higher IGF-II ($P < 0.05$) plasma levels. The maximal response of fetal pituitary cells to GRF was increased ($P < 0.001$). GRF treatment had no influence on maternal and fetal pituitary cell responses to somatostatin under either basal or GRF-stimulated conditions. In addition, these treatments did not affect plasma levels of placental lactogen, glucose, or free fatty acids in the maternal and fetal sheep. These data are compatible with the hypothesis that treatment of pregnant ewes in the last days of gestation with GRF could support accelerated fetal growth.

L3 ANSWER 48 OF 49 MEDLINE on STN DUPLICATE 33
ACCESSION NUMBER: 91031229 MEDLINE
DOCUMENT NUMBER: PubMed ID: 2226300
TITLE: Insulin-like growth factor II is a potent inhibitor of the aromatase activity of human placental cytotrophoblasts.
AUTHOR: Nestler J E
CORPORATE SOURCE: Division of Endocrinology and Metabolism, Medical College of Virginia/Virginia Commonwealth University, Richmond 23298.
SOURCE: Endocrinology, (1990 Nov) Vol. 127, No. 5, pp. 2064-70. Journal code: 0375040. ISSN: 0013-7227.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199012
ENTRY DATE: Entered STN: 8 Feb 1991
Last Updated on STN: 3 Feb 1997
Entered Medline: 4 Dec 1990

AB The placenta is the primary source of estrogens and progesterone during pregnancy. Because pregnant diabetic women are reported to have lower serum estrogen and higher progesterone levels than nondiabetic pregnant women, and placental insulin-like growth factor II (IGF-II) production may be elevated during diabetic pregnancy, the role of IGF-II in the regulation of human cytotrophoblastic aromatase, 3 beta-hydroxysteroid dehydrogenase (3 beta HSD), and P450 cholesterol side-chain cleavage (P450scc) enzyme activities was studied. Incubation of cytotrophoblasts with IGF -II for 24 h significantly diminished the ability of these cells to convert androstenedione to estrogens by 92.3 +/- 6.6 (SE)%. IGF-II could suppress aromatase activity at a concentration as low as 2.0 ng/ml. Preincubation of cells with either insulin, IGF-I, or a monoclonal anti-IGF-I receptor antibody did not alter IGF-II's potent inhibitory effect. Treatment with mannose 6-phosphate alone also resulted in significant suppression of aromatase activity, and concurrent treatment with both mannose 6-phosphate and IGF-II resulted in greater inhibition than with either agent alone. These observations suggest that IGF -II suppresses aromatase activity by activation of its own specific receptor. In contrast, incubation of cytotrophoblasts with IGF-II for 24 h significantly increased the 3 beta HSD activity (as determined by the conversion of pregnenolone to progesterone) and P450scc activity (as determined by the conversion of 25-hydroxycholesterol to progesterone) of these cells. IGF-II's ability to stimulate these enzymatic processes was found to be comparable in magnitude to that of IGF-I. IGF-II -stimulated 3 beta HSD activity was completely inhibited by concurrent treatment with either actinomycin D or cycloheximide, suggesting that new mRNA and protein synthesis are required for IGF-II to exert its stimulatory effect. These studies indicate that IGF-II is a potent inhibitor of human cytotrophoblastic aromatase activity in vitro. In addition, IGF-II can stimulate cytotrophoblastic 3 beta HSD and P450scc activities. Since placental IGF-II production in pregnant diabetic women may be augmented, these observations may help explain the lower serum estrogen and higher progesterone levels associated with pregnancy in the diabetic patient.

L3 ANSWER 49 OF 49 MEDLINE on STN DUPLICATE 34
ACCESSION NUMBER: 90237714 MEDLINE
DOCUMENT NUMBER: PubMed ID: 2159044
TITLE: Effects of passive immunization of growing guinea-pigs with an insulin-like growth factor-I monoclonal antibody.

AUTHOR: Kerr D E; Laarveld B; Manns J G
CORPORATE SOURCE: Department of Veterinary Physiological Sciences, University of Saskatchewan, Saskatoon, Canada.
SOURCE: The Journal of endocrinology, (1990 Mar) Vol. 124, No. 3, pp. 403-15.
Journal code: 0375363. ISSN: 0022-0795.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199006
ENTRY DATE: Entered STN: 6 Jul 1990
Last Updated on STN: 6 Jul 1990
Entered Medline: 7 Jun 1990

AB The physiological importance of circulating as opposed to locally produced insulin-like growth factor-I (IGF-I) has not been determined. By using a passive immunoneutralization technique, our objectives were to evaluate the role of circulating IGF-I in the regulation of animal growth and pituitary GH content. A monoclonal antibody (MAb) to IGF-I, generated in our laboratory, has an affinity (Ka) of 0.13 litres/pmol for recombinant human IGF-I (rhIGF-I). Cross-reactivities of recombinant des-tripeptide IGF-I and recombinant bovine IGF-II were approximately 40 and 8% respectively. This MAb inhibited binding of purified hIGF-I to human placental membranes. In a radioimmunoassay based on displacement of 125I-labelled rhIGF-I from the MAb, displacement curves generated with dilutions of acid-gel chromatography extracts of guinea-pig serum and rhIGF-I standards were parallel. Twenty-four, 3-week-old male guinea-pigs were treated with the IGF-I MAb, a bovine herpes virus-I (BHV-I) MAb (control MAb) or vehicle (phosphate-buffered saline) (n = 8 per group). Treatments were administered i.p. every 3 days for 24 days at a dose of 20 mg/kg body weight. Blood was obtained on day 23 (48 h after treatment) and on day 25 (24 h after treatment). In a liquid-phase assay, serum from the IGF-I MAb-treated group bound 38 +/- 8% (mean +/- S.E.M.) (day 23) and 56 +/- 7% (day 25) of an 125I-labelled rhIGF-I trace at a final dilution of 1:10,000. Because of the development of an anti-mouse immune response in the guinea-pigs, these parameters would probably have been much greater during the first 2 weeks of the trial. Of the total IGF-I in serum, 50 +/- 5% and 61 +/- 4% could be immunoprecipitated with an excess of rabbit anti-mouse immunoglobulin in samples from days 23 and 25 respectively. Comparisons between the groups treated with IGF-I MAb and BHV-I MAb revealed no significant differences in whole animal growth rate, growth of individual tissues, or pituitary GH content. Mean serum concentrations of IGF-I were 69 and 99% greater in the IGF-I MAb-treated group than in the BHV-I MAb-treated group on days 23 and 25 respectively. These differences probably resulted from an extension of the half-life of IGF-I in serum of animals treated with the IGF-I MAb.(ABSTRACT TRUNCATED AT 400 WORDS)

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